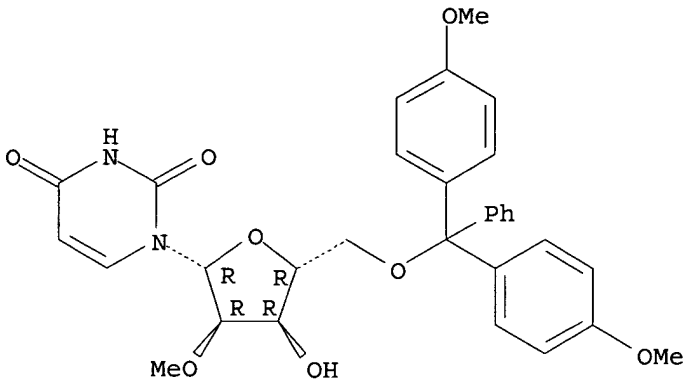
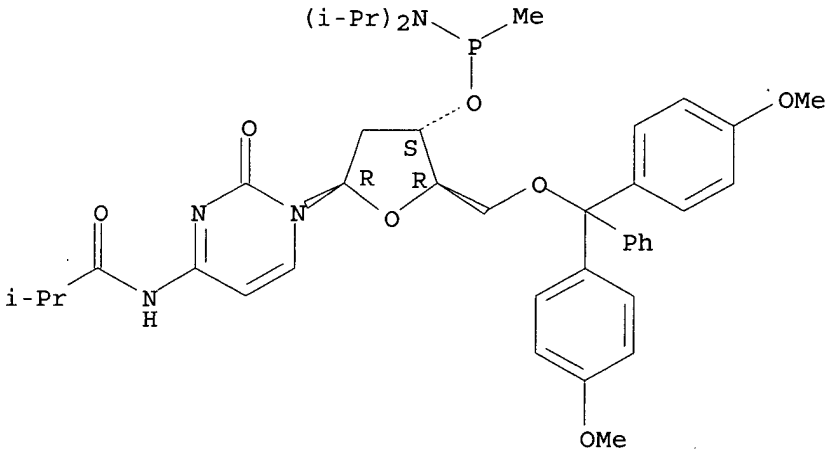


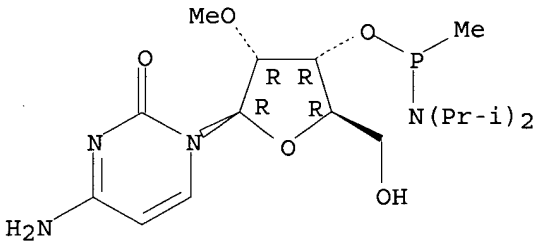
RN 128192-22-3 HCAPLUS
CN Cytidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-N-(2-methyl-1-oxopropyl)-, 3'-[P-methyl-N,N-bis(1-methylethyl)phosphonamidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



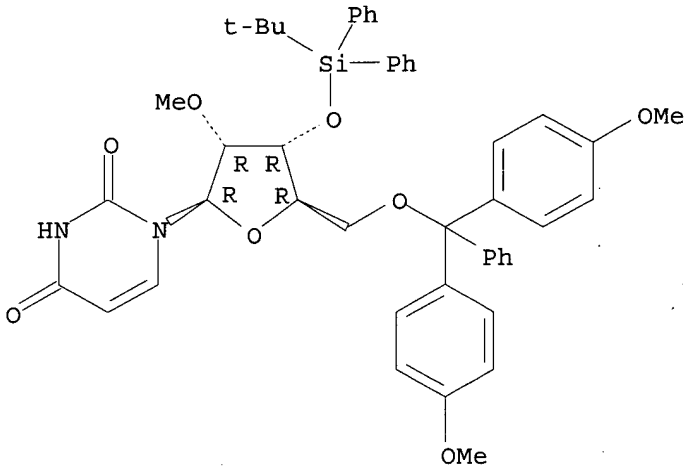
IT **168635-65-2P 168635-66-3P 168635-67-4P**
168635-68-5P 168635-70-9P 168635-71-0P
168635-72-1P 168635-83-4P 168635-84-5P
168752-52-1P 168752-53-2P 168752-54-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and use in preventing formation or translation of RNA of **chirally** enriched synthetic phosphonate **oligonucleotides**)
RN 168635-65-2 HCAPLUS
CN Cytidine, 2'-O-methyl-, 3'-[P-methyl-N,N-bis(1-methylethyl)phosphonamidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



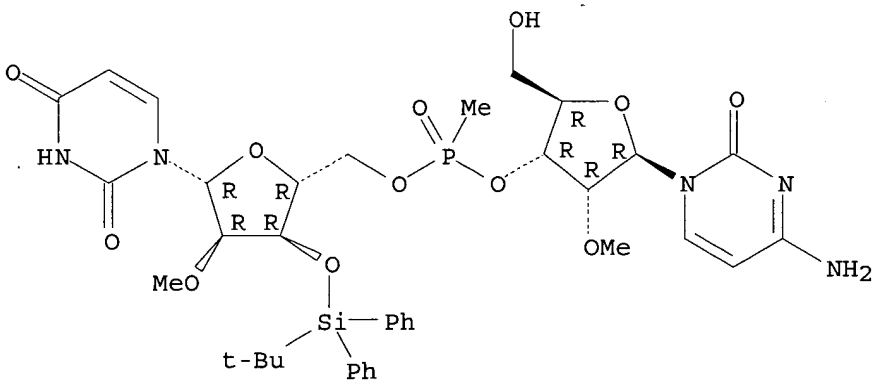
RN 168635-66-3 HCAPLUS
CN Uridine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-3'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 168635-67-4 HCAPLUS
CN Uridine, P-deoxy-P-methyl-2'-O-methylcytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

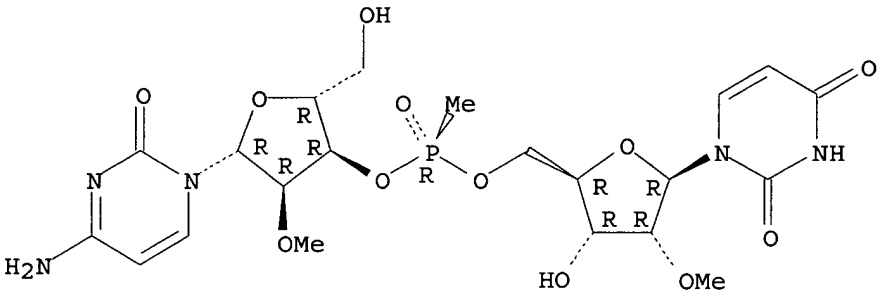
Absolute stereochemistry.



RN 168635-68-5 HCAPLUS

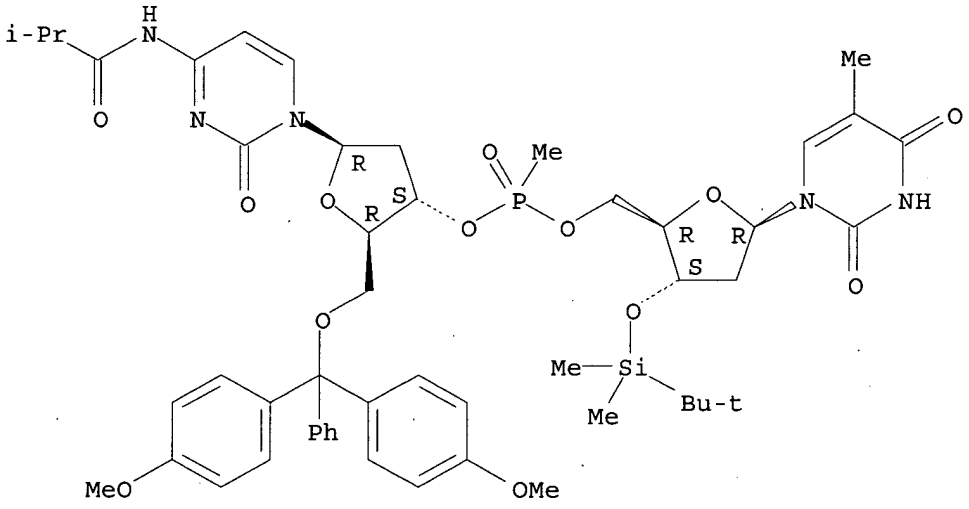
CN Uridine, (R)-P-deoxy-P-methyl-2'-O-methylcytidylyl-(3'→5')-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



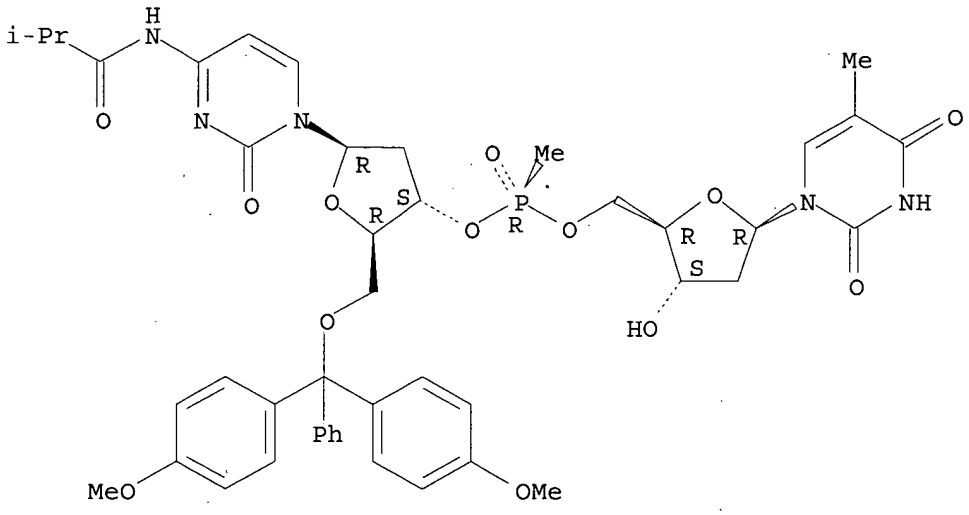
RN 168635-70-9 HCAPLUS
CN Thymidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P,2'-dideoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



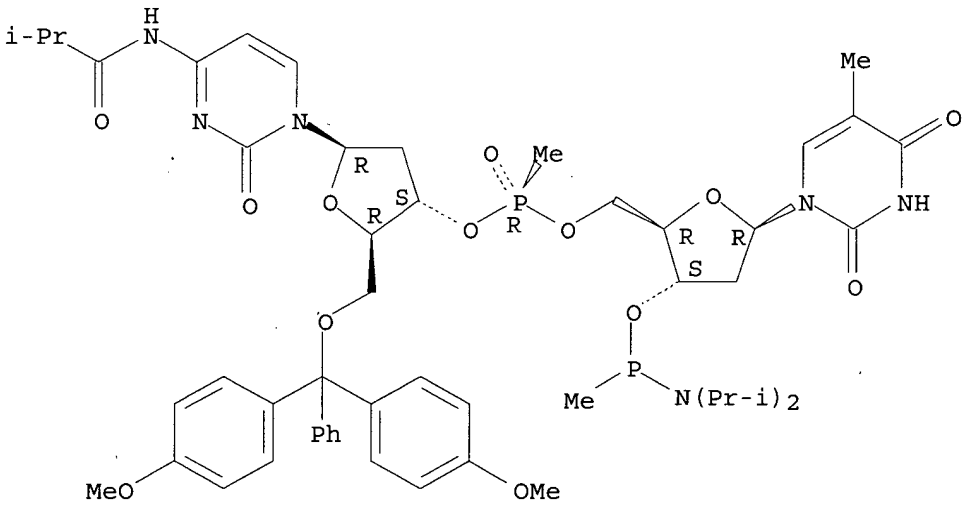
RN 168635-71-0 HCAPLUS
CN Thymidine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P,2'-dideoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



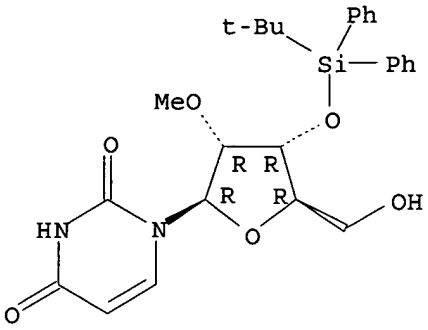
RN 168635-72-1 HCAPLUS
CN Thymidine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P,2'-dideoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-, 3'-[P-methyl-N,N-bis(1-methylethyl)phosphonamidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



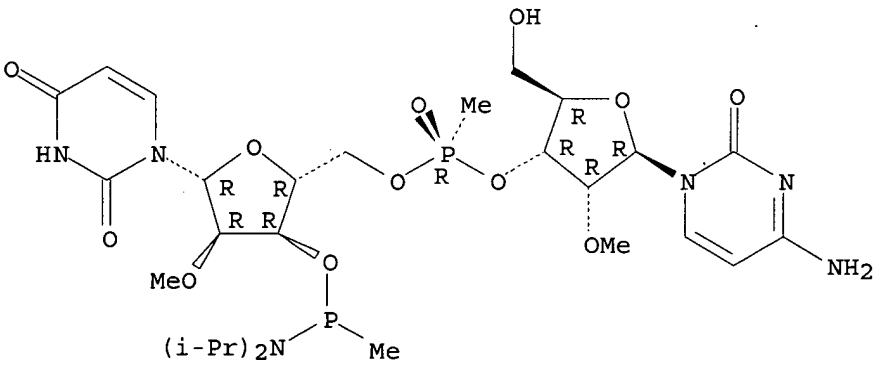
RN 168635-83-4 HCAPLUS
CN Uridine, 3'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



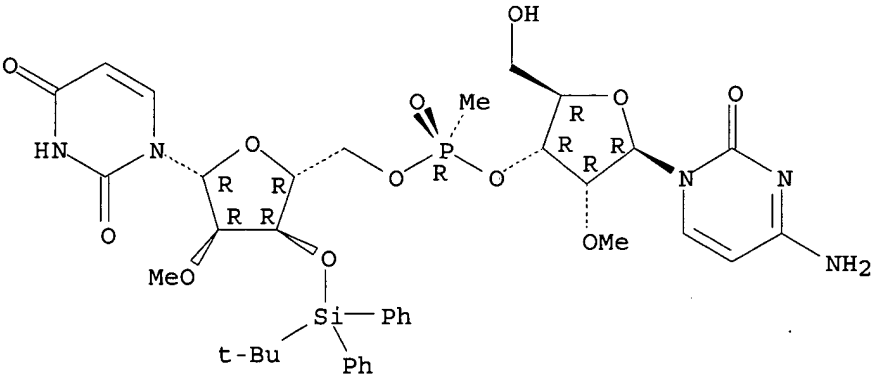
RN 168635-84-5 HCAPLUS
CN Uridine, (R)-P-deoxy-P-methyl-2'-O-methylcytidylyl-(3'→5')-2'-O-methyl-, 3'-[P-methyl-N,N-bis(1-methylethyl)phosphonamidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 168752-52-1 HCAPLUS
CN Uridine, (R)-P-deoxy-P-methyl-2'-O-methylcytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

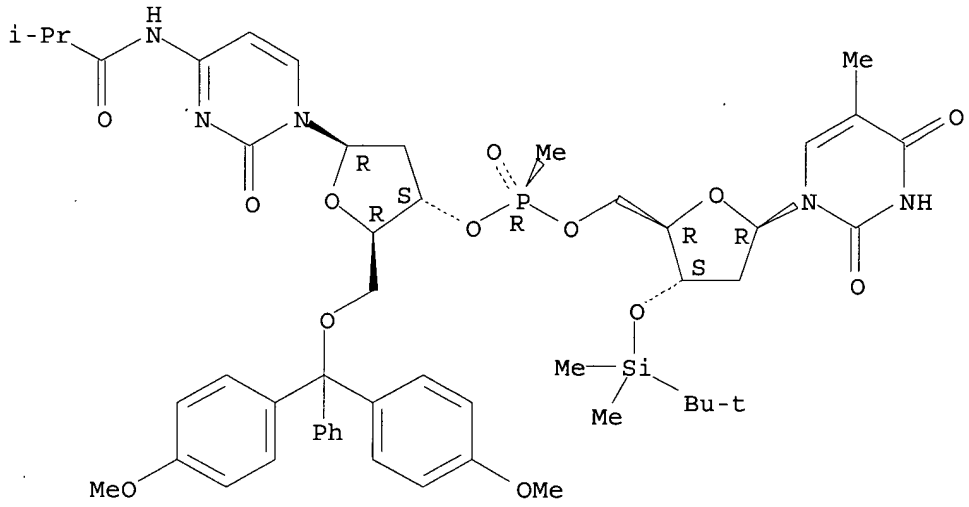
Absolute stereochemistry.



RN 168752-53-2 HCAPLUS

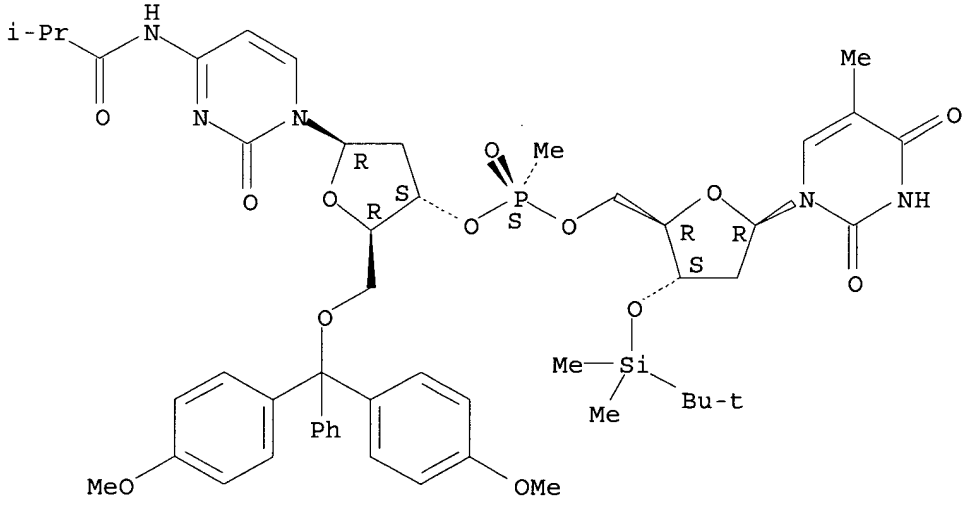
CN Thymidine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 168752-54-3 HCAPLUS
CN Thymidine, [P(S)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 22 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:837553 HCAPLUS
DOCUMENT NUMBER: 123:248528
TITLE: Synthetic oligomers having **chirally** pure phosphonate **internucleosidyl** linkages mixed with non-phosphonate **internucleosidyl**

linkages: their preparation and use in preventing formation or translation of RNA
INVENTOR(S): Arnold, Lyle John, Jr.; Hogrefe, Richard Isais; Reynolds, Mark Alan; Riley, Timothy Andrew; Schwartz, David Aaron; Vaghefi, Morteza Monir; Brown, Bob Dale
PATENT ASSIGNEE(S): Genta Inc., USA
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9514030	A1	19950526	WO 1994-US13341	19941116
W: AU, CA, JP, KR, NZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2176256	AA	19950526	CA 1994-2176256	19941116
AU 9511819	A1	19950606	AU 1995-11819	19941116
AU 678085	B2	19970515		
EP 729474	A1	19960904	EP 1995-902609	19941116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09507836	T2	19970812	JP 1995-514623	19941116
IL 128658	A1	20030312	IL 1994-128658	19941116
US 5792615	A	19980811	US 1997-812861	19970306
US 6060456	A	20000509	US 1997-960111	19971027

PRIORITY APPLN. INFO.:		
US 1993-154014	A	19931116
US 1993-154013	A	19931116
US 1994-233778	A	19940426
US 1994-238177	A	19940504
IL 1994-111660	A3	19941116
WO 1994-US13341	W	19941116
US 1995-481637	B1	19950607

OTHER SOURCE(S): MARPAT 123:248528
ED Entered STN: 07 Oct 1995
AB Oligomers having **chirally** pure phosphonate **internucleosidyl** linkages mixed with non-phosphonate **internucleosidyl** linkages which hybridize to RNA target sequences and methods for their preparation are provided. **Dinucleotide** synthons containing Rp methylphosphonate linkages and **oligonucleotides** containing Rp methylphosphonate linkages alternating with phosphodiester linkages were prepared Resistance to nuclease digestion and the ability of antisense **oligonucleotides** of the invention to inhibit in vitro protein synthesis were demonstrated.
IC ICM C07H021-04
ICS A61K048-00
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 33
ST **oligonucleotide chiral** methylphosphonate linkage synthesis; RNA biosynthesis translation methylphosphonate linked **oligonucleotide**
IT **Transcription, genetic**
Translation, genetic
(preparation and use in preventing formation or translation of RNA of synthetic oligomers having **chiral** phosphonate and non-phosphonate **internucleosidyl** linkages)
IT **Nucleotides, biological studies**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(**oligo-**, **chiral** methylphosphonate-linked; preparation and use in preventing formation or translation of RNA of synthetic oligomers having **chiral** phosphonate and non-phosphonate **internucleosidyl** linkages)

IT 168758-37-0P 168758-38-1P 168758-39-2P 168758-40-5P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and use in preventing formation or translation of RNA of synthetic oligomers having **chiral** phosphonate and non-phosphonate **internucleosidyl** linkages)

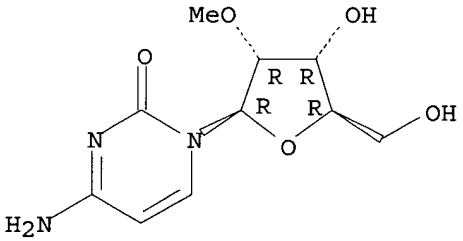
IT 58-96-8, Uridine **2140-72-9 40733-27-5** 51747-24-1
58479-61-1 89992-70-1 **103285-22-9** 114745-26-5
128192-22-3 153809-39-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and use in preventing formation or translation of RNA of synthetic oligomers having **chiral** phosphonate and non-phosphonate **internucleosidyl** linkages)

IT **168635-65-2P 168635-66-3P 168635-67-4P**
168635-68-5P 168635-69-6P 168635-70-9P
168635-71-0P 168635-72-1P 168635-73-2P 168635-74-3P
168635-75-4P 168635-76-5P **168635-77-6P 168635-78-7P**
168635-79-8P **168635-80-1P 168635-81-2P**
168635-82-3P 168635-83-4P 168752-52-1P
168752-53-2P 168752-54-3P 168752-55-4P
168752-56-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and use in preventing formation or translation of RNA of synthetic oligomers having **chiral** phosphonate and non-phosphonate **internucleosidyl** linkages)

IT **2140-72-9 40733-27-5 103285-22-9**
128192-22-3 153809-39-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and use in preventing formation or translation of RNA of synthetic oligomers having **chiral** phosphonate and non-phosphonate **internucleosidyl** linkages)

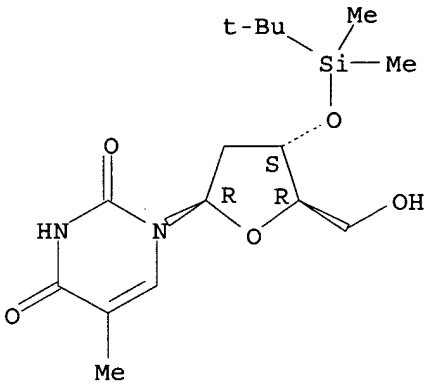
RN 2140-72-9 HCAPLUS
CN Cytidine, 2'-O-methyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



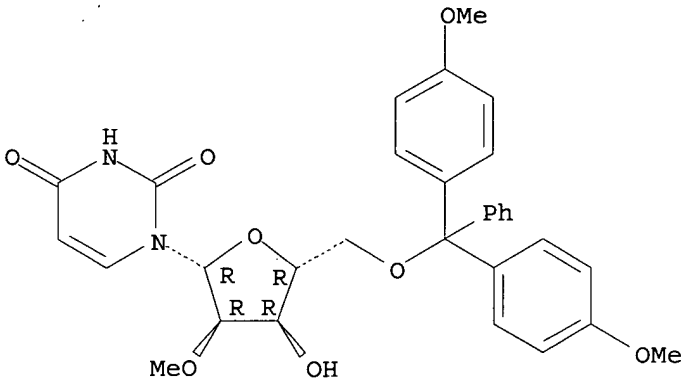
RN 40733-27-5 HCAPLUS
CN Thymidine, 3'-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



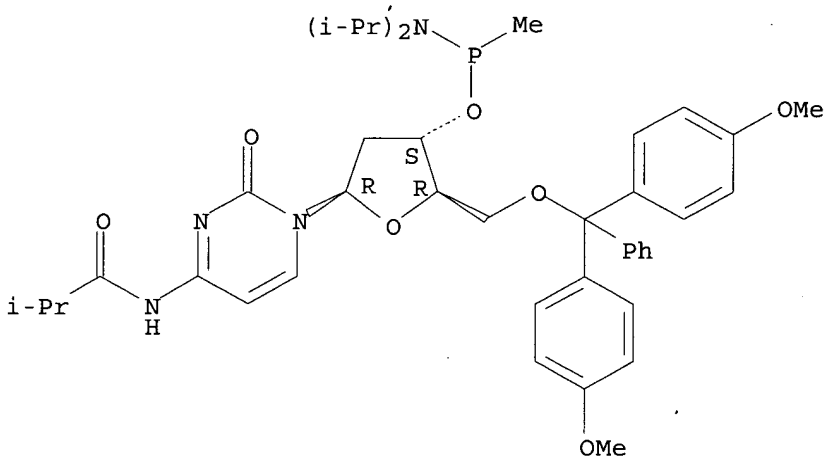
RN 103285-22-9 HCAPLUS
CN Uridine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



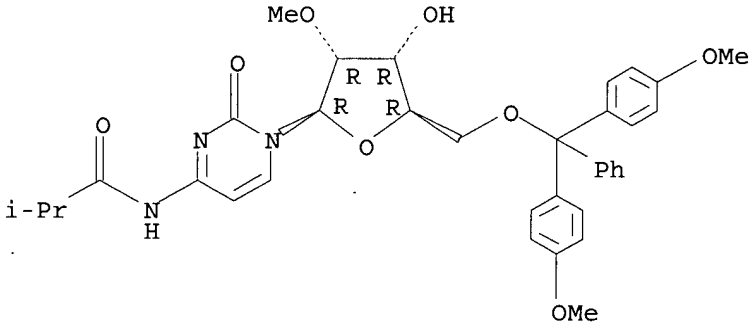
RN 128192-22-3 HCAPLUS
CN Cytidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-N-(2-methyl-1-oxopropyl)-, 3'-[P-methyl-N,N-bis(1-methylethyl)phosphonamidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



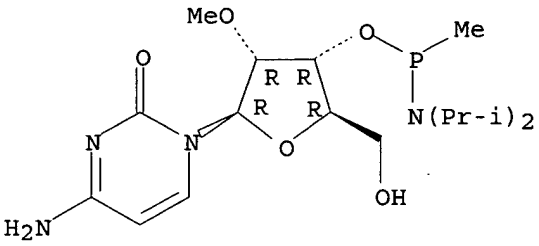
RN 153809-39-3 HCAPLUS
CN Cytidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyl-N-(2-methyl-1-oxopropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



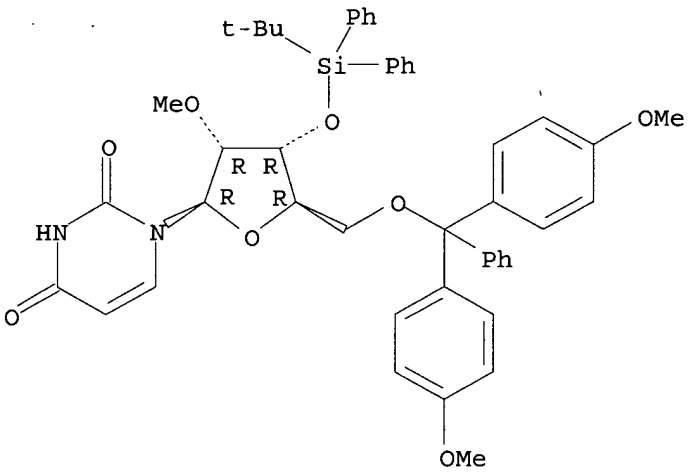
IT **168635-65-2P 168635-66-3P 168635-67-4P**
168635-68-5P 168635-69-6P 168635-70-9P
168635-71-0P 168635-72-1P 168635-77-6P
168635-78-7P 168635-80-1P 168635-81-2P
168635-82-3P 168635-83-4P 168752-52-1P
168752-53-2P 168752-54-3P 168752-56-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and use in preventing formation or translation of RNA of synthetic oligomers having **chiral** phosphonate and non-phosphonate **internucleosidyl** linkages)
RN 168635-65-2 HCAPLUS
CN Cytidine, 2'-O-methyl-, 3'-[P-methyl-N,N-bis(1-methylethyl)phosphonamidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



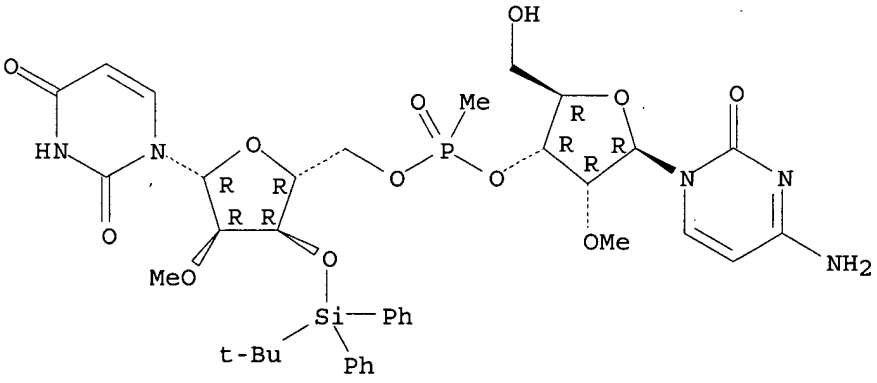
RN 168635-66-3 HCAPLUS
CN Uridine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-3'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 168635-67-4 HCAPLUS
CN Uridine, P-deoxy-P-methyl-2'-O-methylcytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

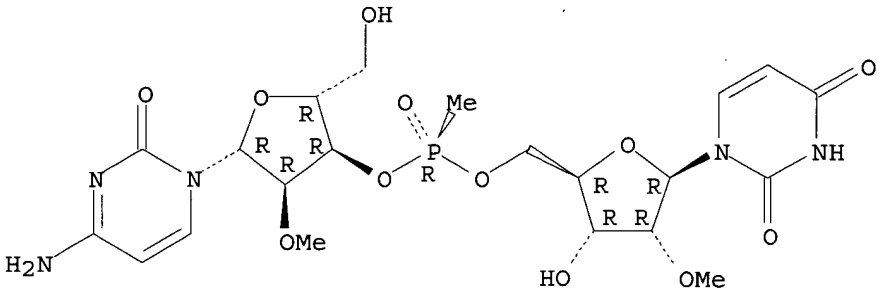
Absolute stereochemistry.



RN 168635-68-5 HCAPLUS

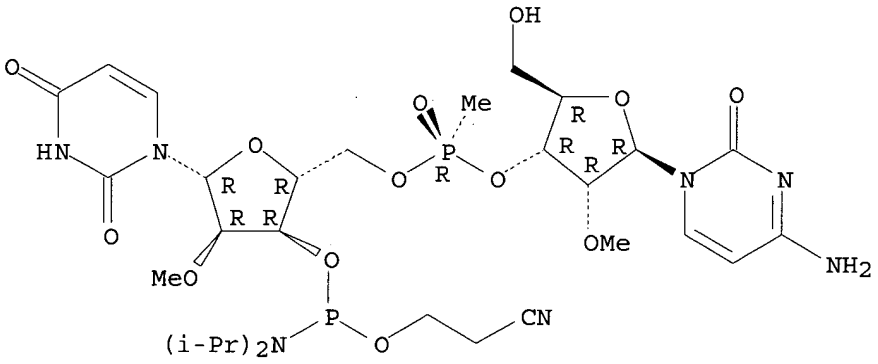
CN Uridine, (R)-P-deoxy-P-methyl-2'-O-methylcytidylyl-(3'→5')-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



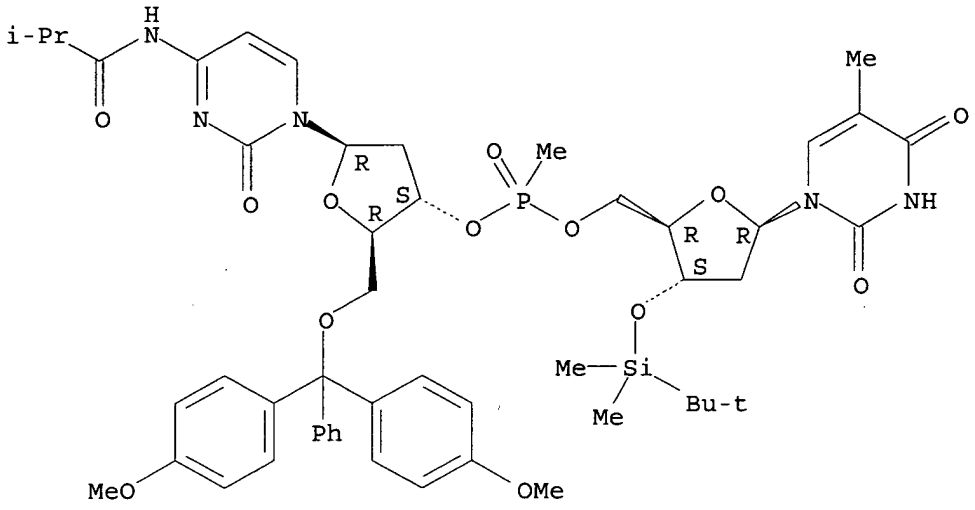
RN 168635-69-6 HCAPLUS
CN Uridine, (R)-P-deoxy-P-methyl-2'-O-methylcytidylyl-(3'→5')-2'-O-methyl-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



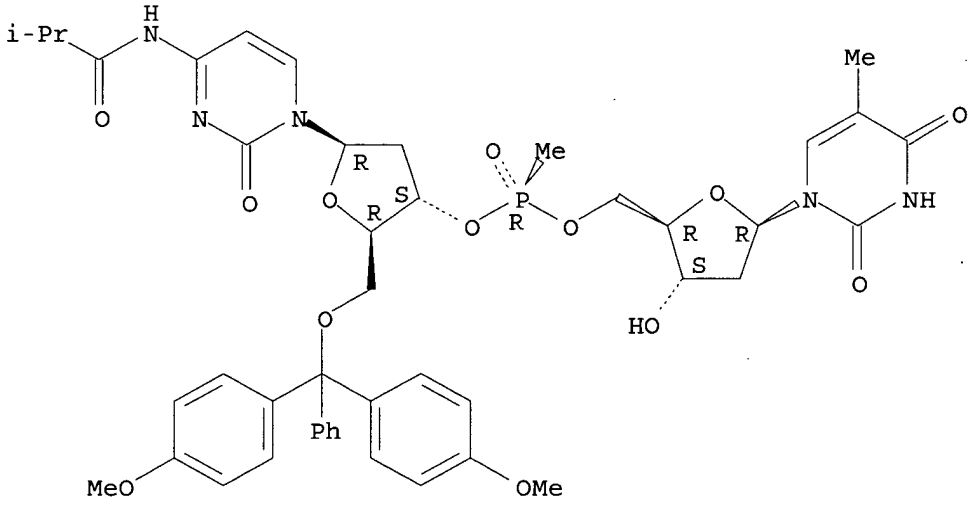
RN 168635-70-9 HCAPLUS
CN Thymidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P,2'-dideoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



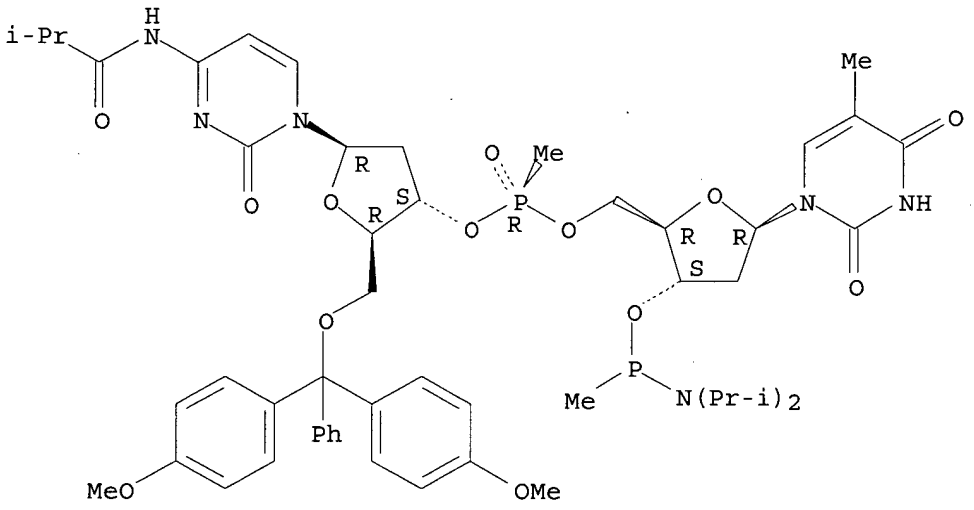
RN 168635-71-0 HCAPLUS
CN Thymidine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P,2'-dideoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



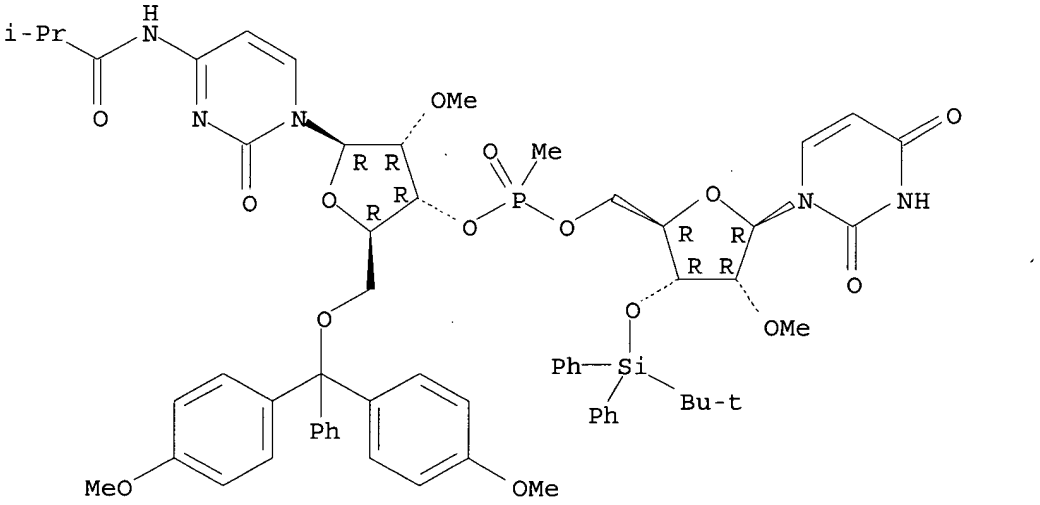
RN 168635-72-1 HCAPLUS
CN Thymidine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P,2'-dideoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-, 3'-[P-methyl-N,N-bis(1-methylethyl)phosphonamidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



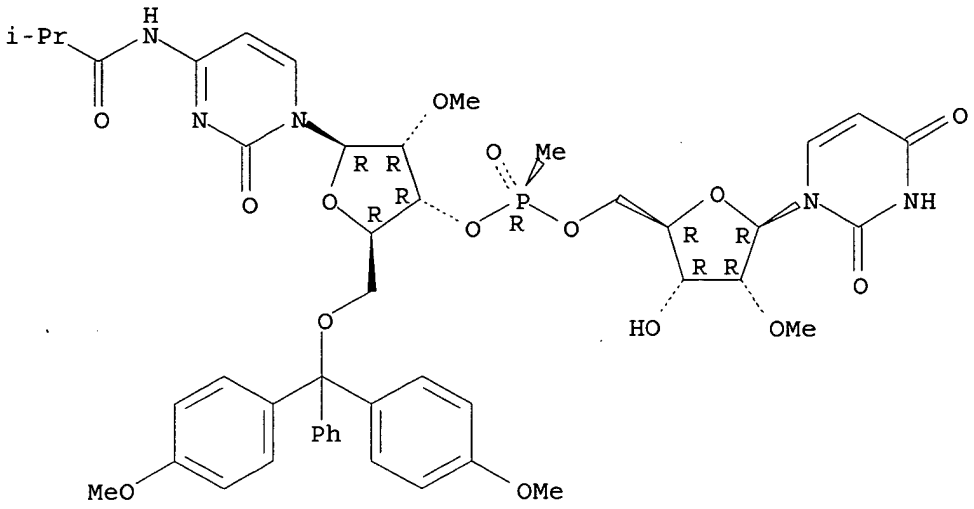
RN 168635-77-6 HCAPLUS
CN Uridine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-2'-O-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-3-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



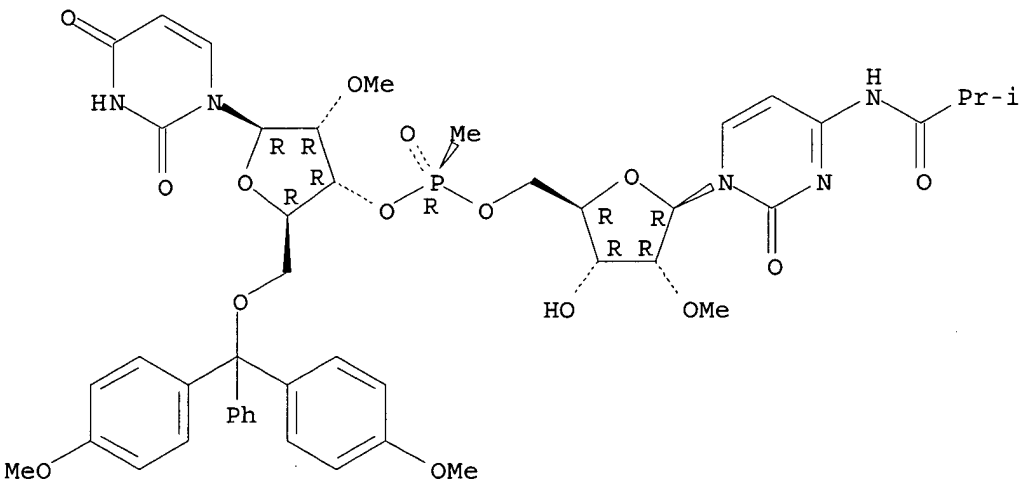
RN 168635-78-7 HCAPLUS
CN Uridine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-2'-O-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



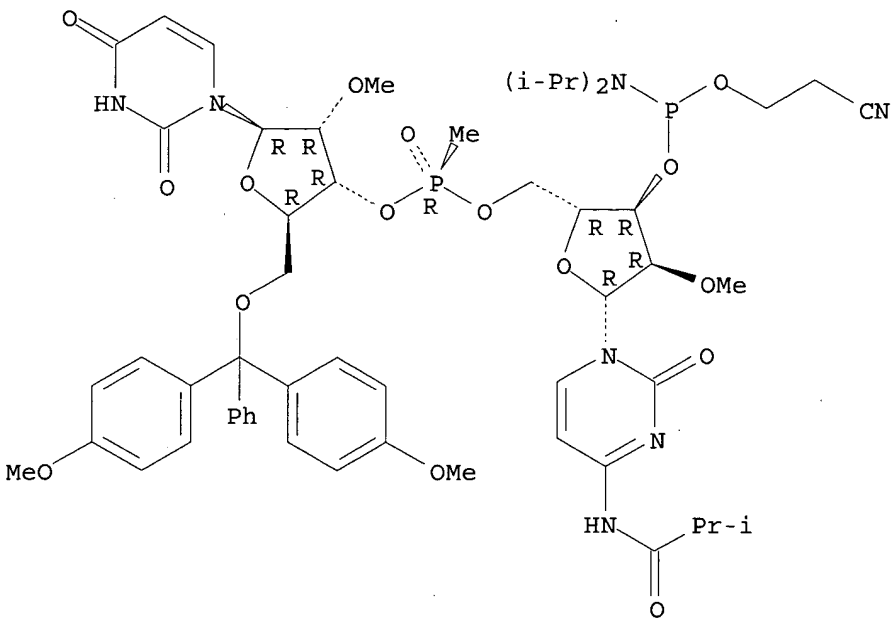
RN 168635-80-1 HCAPLUS
CN Cytidine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-2'-O-methyluridylyl-(3'→5')-2'-O-methyl-N-(2-methyl-1-oxopropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



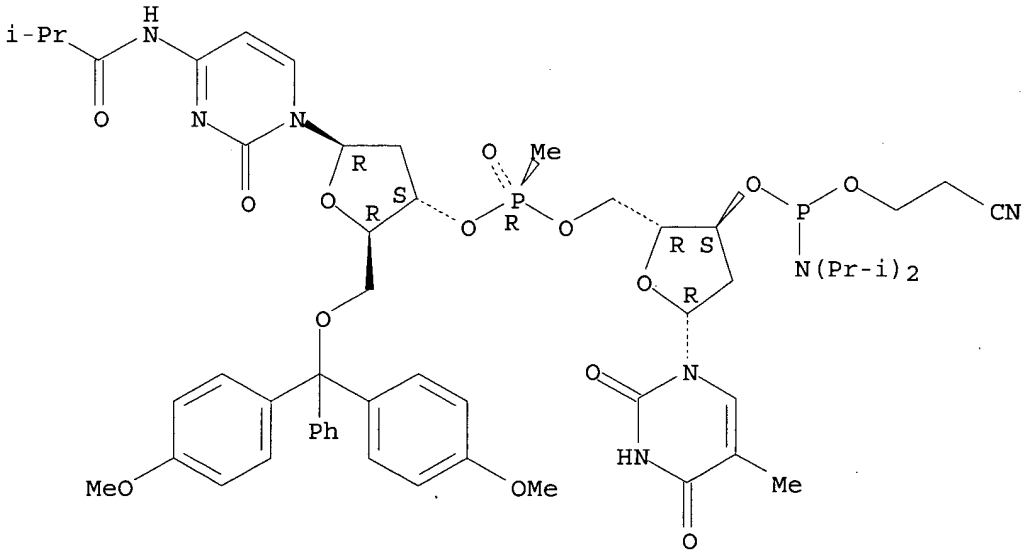
RN 168635-81-2 HCAPLUS
CN Cytidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-2'-O-methyluridylyl-(3'→5')-2'-O-methyl-N-(2-methyl-1-oxopropyl)-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



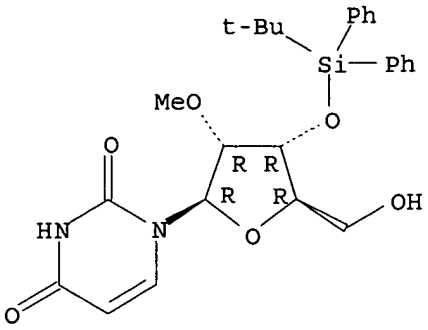
RN 168635-82-3 HCAPLUS
CN Thymidine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P,2'-dideoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



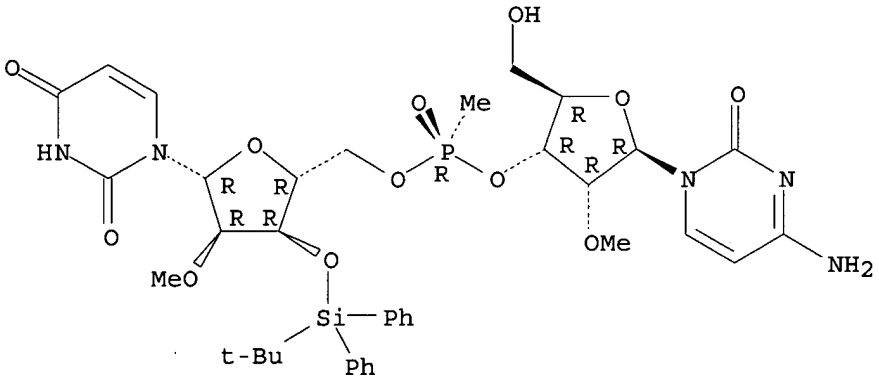
RN 168635-83-4 HCAPLUS
CN Uridine, 3'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



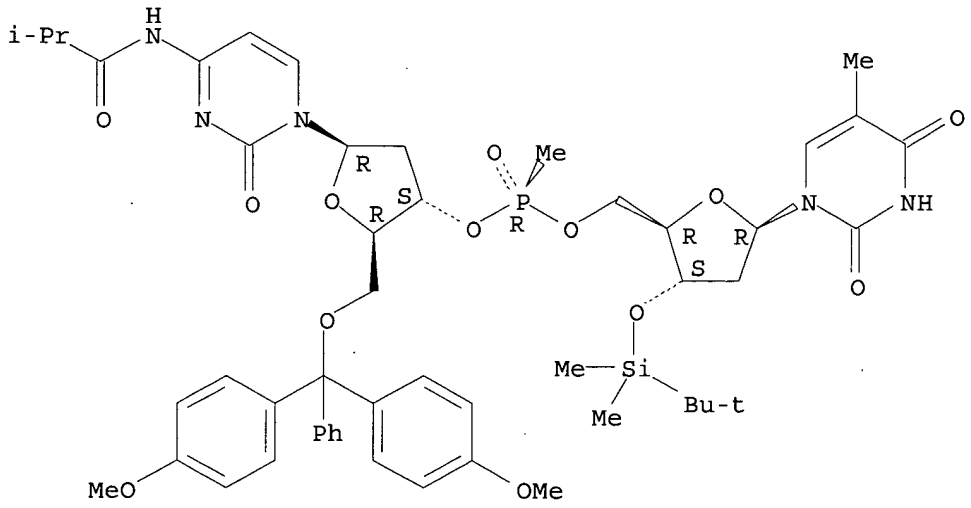
RN 168752-52-1 HCAPLUS
CN Uridine, (R)-P-deoxy-P-methyl-2'-O-methylcytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



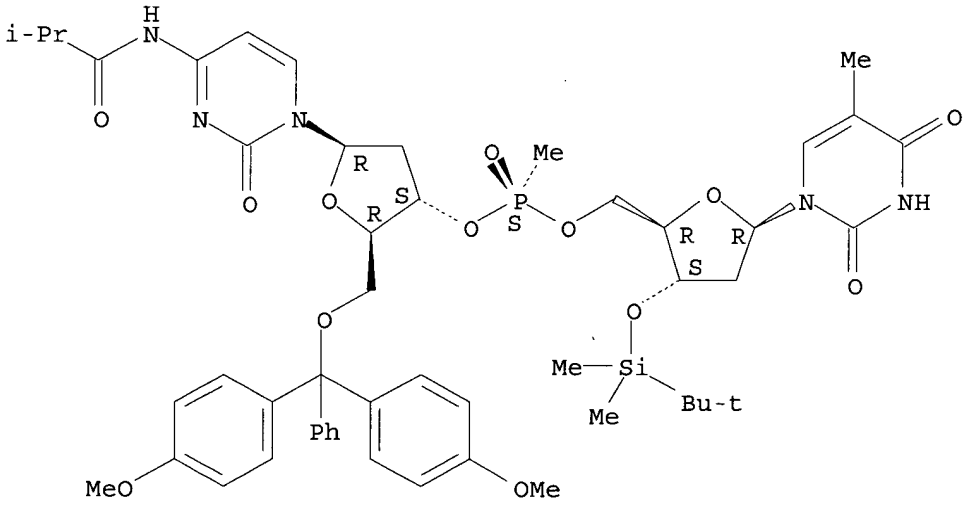
RN 168752-53-2 HCAPLUS
CN Thymidine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



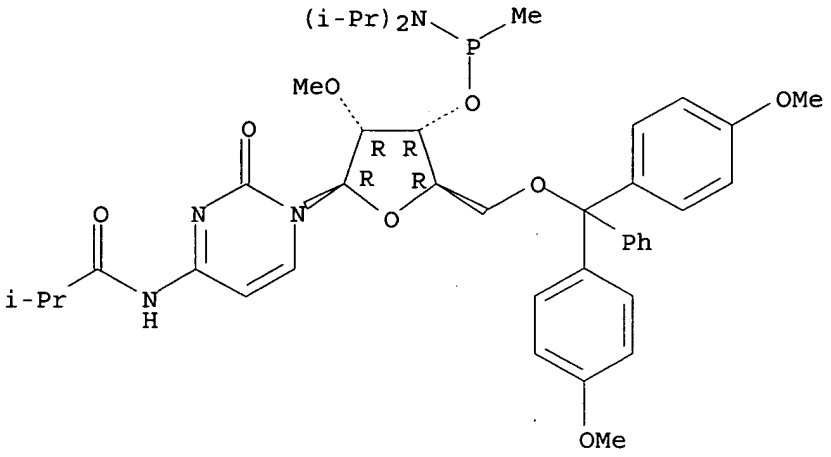
RN 168752-54-3 HCAPLUS
CN Thymidine, [P(S)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 168752-56-5 HCAPLUS
CN Cytidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyl-N-(2-methyl-1-oxopropyl)-, 3'-[P-methyl-N,N-bis(1-methylethyl)phosphonamidate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 23 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:858610 HCAPLUS
DOCUMENT NUMBER: 123:248527
TITLE: Chimeric RNase H-activating oligonucleotides and their use in pharmaceuticals
INVENTOR(S): Arnold, Lyle J., Jr.; Reynolds, Mark A.; Giachetti, Christina
PATENT ASSIGNEE(S): Genta, Inc., USA
SOURCE: PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9513834	A1	19950526	WO 1994-US13387	19941116
W: AU, CA, JP, KR, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2176259	AA	19950526	CA 1994-2176259	19941116
AU 9512916	A1	19950606	AU 1995-12916	19941116
AU 689182	B2	19980326		
EP 743859	A1	19961127	EP 1995-904098	19941116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09506248	T2	19970624	JP 1994-514646	19941116
IL 128658	A1	20030312	IL 1994-128658	19941116
WO 9528942	A1	19951102	WO 1995-US5179	19950425
W: AU, CA, JP, KR, NZ				
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AU 9525843	A1	19951116	AU 1995-25843	19950425
US 5955597	A	19990921	US 1997-885126	19970630
US 6060456	A	20000509	US 1997-960111	19971027
US 6262036	B1	20010717	US 2000-490774	20000124
PRIORITY APPLN. INFO.:			US 1993-154013 A	19931116
			US 1993-154014 A	19931116
			US 1994-233778 A	19940426
			US 1994-238177 A	19940504
			IL 1994-111660 A3	19941116
			WO 1994-US13387 W	19941116

US 1994-343018	B1	19941121
US 1994-350431	A	19941205
WO 1995-US5179	W	19950425
US 1995-481637	B1	19950607
US 1997-960111	A3	19971027

ED Entered STN: 17 Oct 1995

AB Chimeric **oligonucleotides** comprising a RNase H-activating region containing 2'-unsubstituted **nucleotides** joined by charged linkages and a non-RNase H-activating region containing some **chiral internucleoside** linkages are disclosed. These chimeric **oligonucleotides** are complementary to a target RNA. The **oligonucleotides** are useful in activating RNaseH-mediated cleavage of target RNA sequences and in treating disease conditions relating to such sequences. Many chimeric **oligonucleotides** were prepared and tested for binding affinity for target RNA, for nuclease resistance, and for stimulation of RNase H cleavage of target RNA. **Expression** of human papilloma virus **genes** in mammalian cells was specifically inhibited by **oligonucleotides** of the invention. Those **oligonucleotides** containing phosphorothioate or alternating phosphorothioate/phosphodiester linkages in a middle region flanked by regions containing alternating **chiral** methylphosphorothioate/methylp hosphonate and phosphodiester linkages were potent inhibitors.

IC ICM A61K048-00
ICS C07H021-02; C07H021-04; C12Q001-68

CC 3-1 (Biochemical Genetics)

IT **Translation, genetic**
(specific inhibition of; chimeric RNase H-activating oligonucleotides and their use in pharmaceuticals)

IT **Nucleotides, biological studies**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**oligo**-, RNase H-activating; chimeric RNase H-activating oligonucleotides and their use in pharmaceuticals)

IT **2140-72-9 40733-27-5** 58479-61-1 89992-70-1
103285-22-9 128192-22-3 168635-65-2
168635-73-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(chimeric RNase H-activating oligonucleotides and their use in pharmaceuticals)

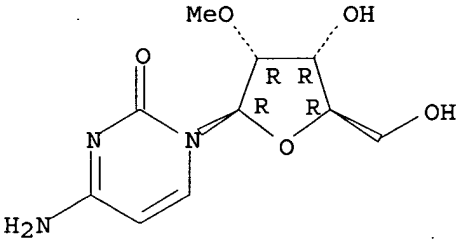
IT 51747-24-1P 114745-26-5P **153809-39-3P 168635-66-3P**
168635-67-4P 168635-68-5P 168635-69-6P
168635-70-9P 168635-71-0P 168635-72-1P
168635-74-3P 168635-75-4P 168635-76-5P **168635-77-6P**
168635-78-7P 168635-79-8P **168635-81-2P**
168635-82-3P 168635-83-4P 168635-84-5P
168752-52-1P 168752-53-2P 168752-54-3P
168752-56-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(chimeric RNase H-activating oligonucleotides and their use in pharmaceuticals)

IT **2140-72-9 40733-27-5 103285-22-9**
128192-22-3 168635-65-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(chimeric RNase H-activating oligonucleotides and their use in pharmaceuticals)

RN 2140-72-9 HCAPLUS

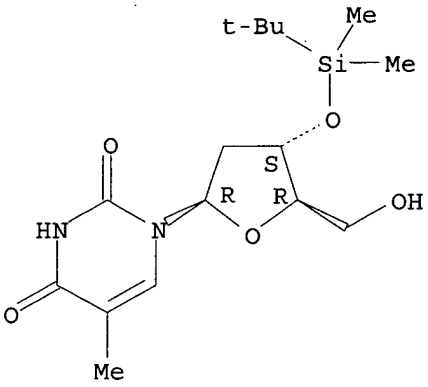
CN Cytidine, 2'-O-methyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



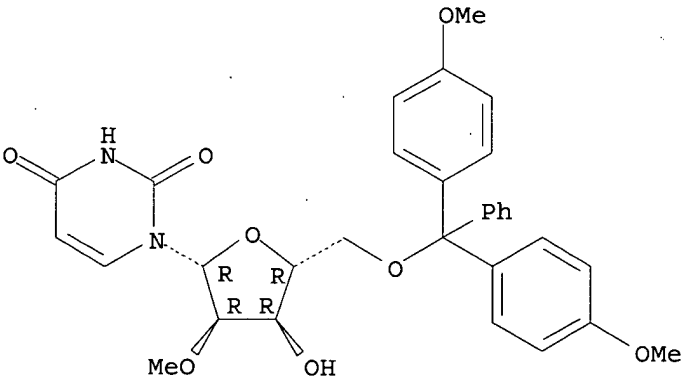
RN 40733-27-5 HCAPLUS
CN Thymidine, 3'-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



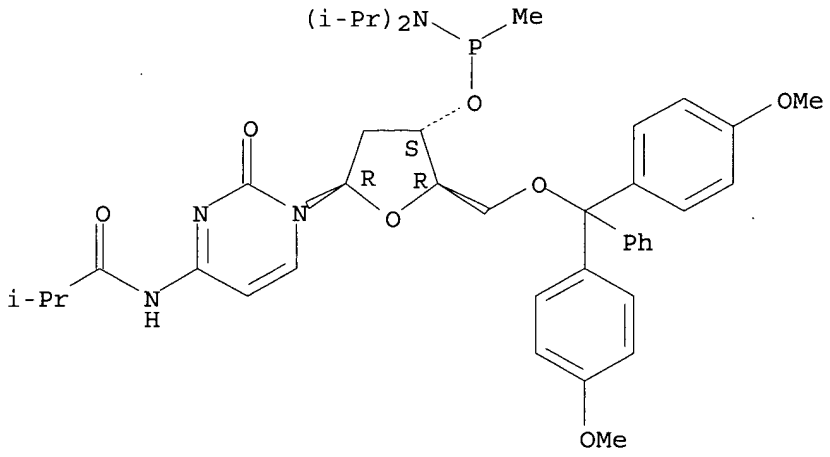
RN 103285-22-9 HCAPLUS
CN Uridine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



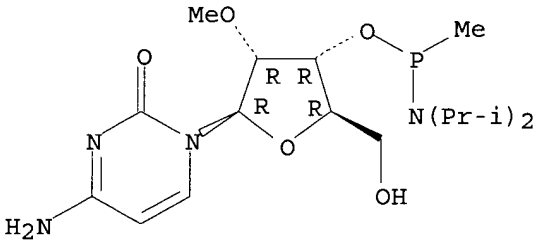
RN 128192-22-3 HCAPLUS
CN Cytidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-N-(2-methyl-1-oxopropyl)-, 3'-[P-methyl-N,N-bis(1-methylethyl)phosphonamidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 168635-65-2 HCAPLUS
CN Cytidine, 2'-O-methyl-, 3'-[P-methyl-N,N-bis(1-methylethyl)phosphonamidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **153809-39-3P 168635-66-3P 168635-67-4P**
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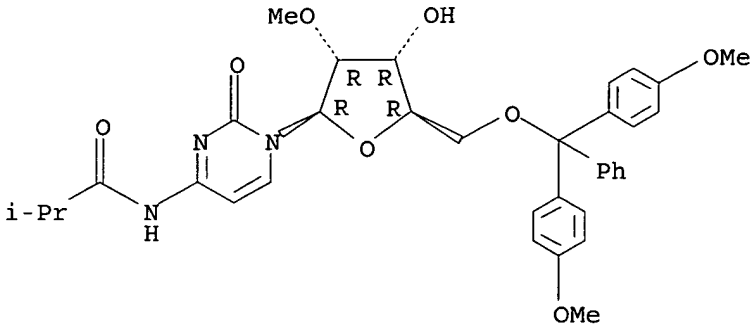
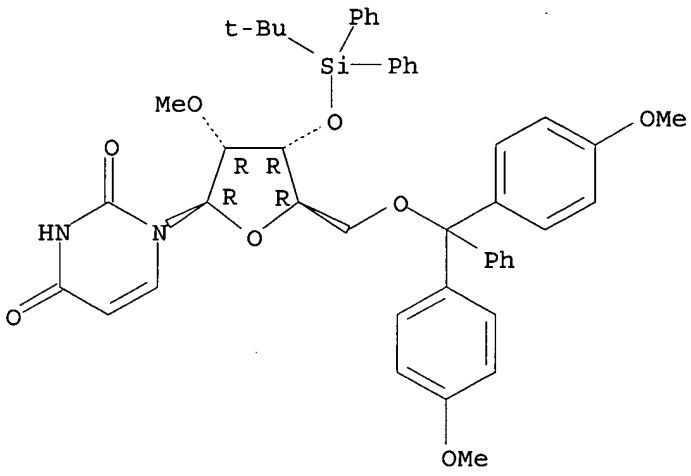
168635-71-0P 168635-72-1P 168635-77-6P
168635-78-7P 168635-81-2P 168635-82-3P
168635-83-4P 168635-84-5P 168752-52-1P
168752-53-2P 168752-54-3P 168752-56-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(chimeric RNase H-activating oligonucleotides and their use in pharmaceuticals)
RN 153809-39-3 HCAPLUS
CN Cytidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyl-N-(2-methyl-1-oxopropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



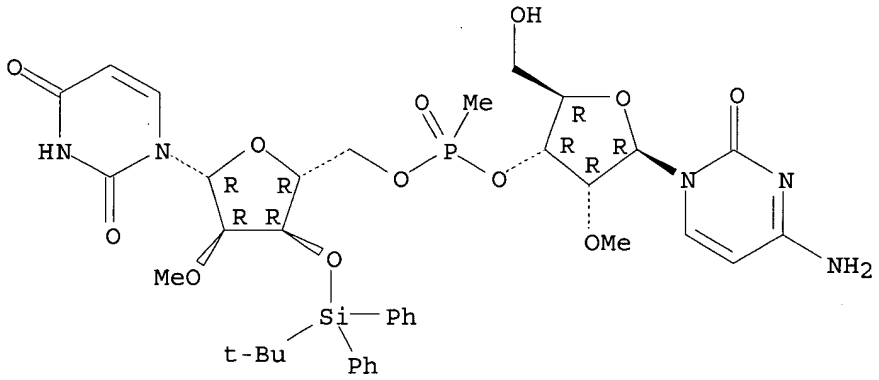
RN 168635-66-3 HCAPLUS
CN Uridine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-3'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



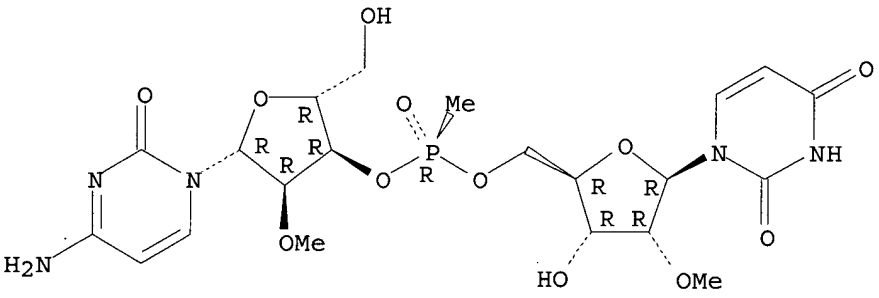
RN 168635-67-4 HCAPLUS
CN Uridine, P-deoxy-P-methyl-2'-O-methylcytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



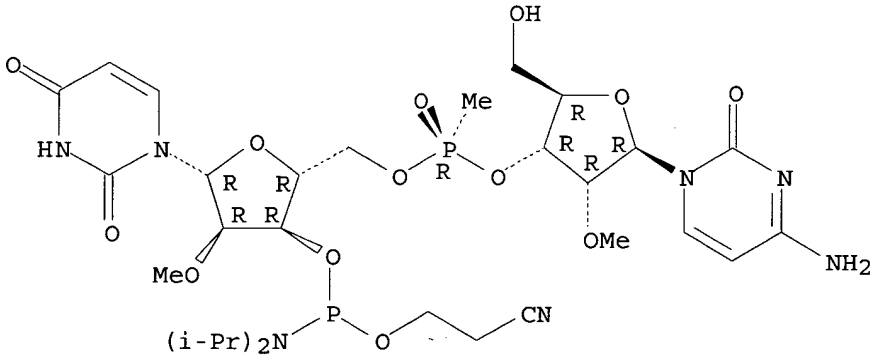
RN 168635-68-5 HCAPLUS
CN Uridine, (R)-P-deoxy-P-methyl-2'-O-methylcytidylyl-(3'→5')-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 168635-69-6 HCAPLUS
CN Uridine, (R)-P-deoxy-P-methyl-2'-O-methylcytidylyl-(3'→5')-2'-O-methyl-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] (9CI) (CA INDEX NAME)

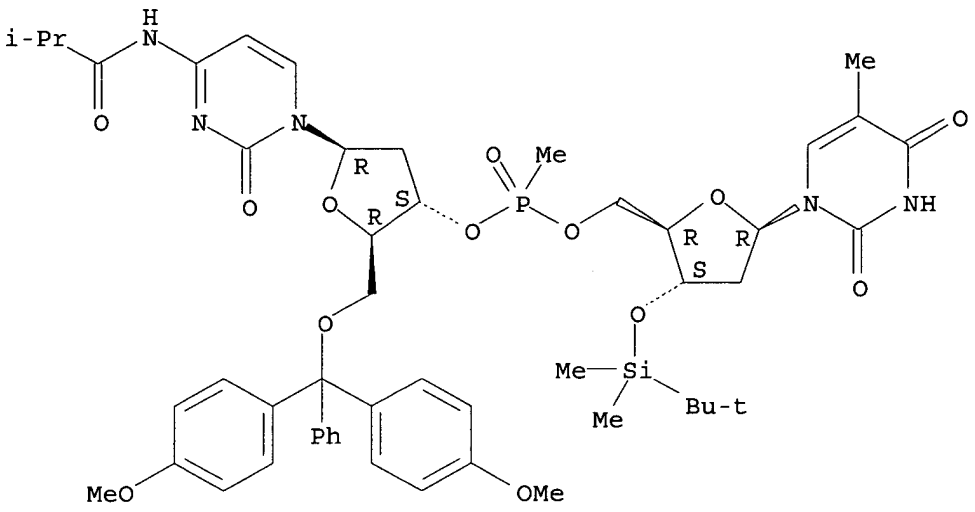
Absolute stereochemistry.



RN 168635-70-9 HCAPLUS
CN Thymidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P,2'-dideoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-3'-O-[(1,1-

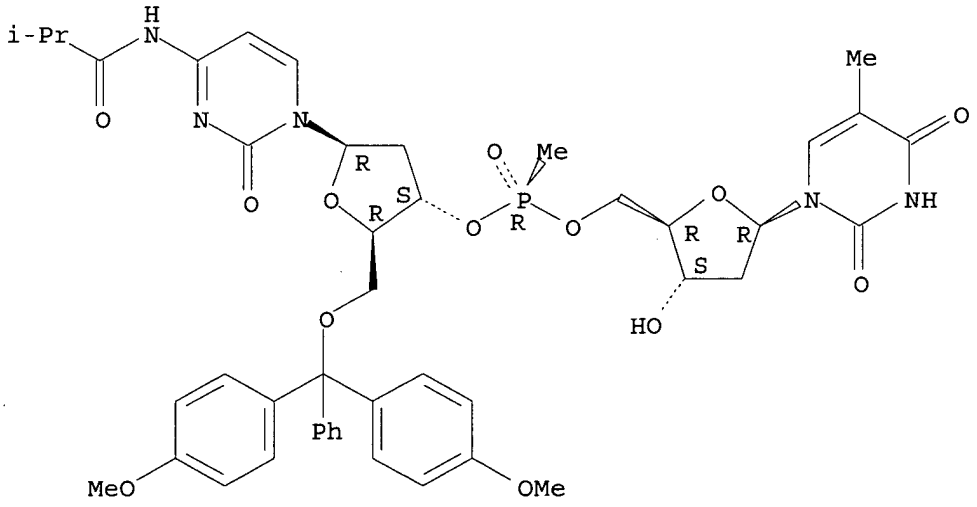
dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



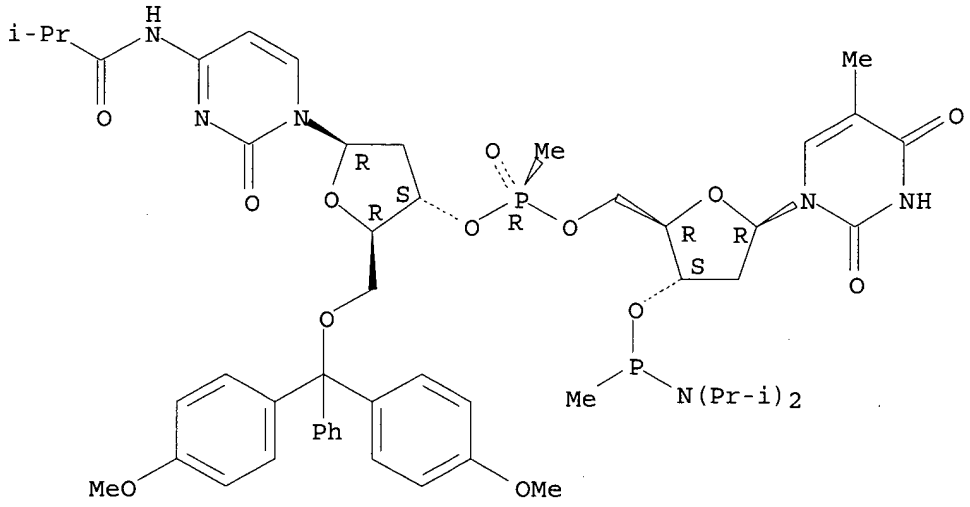
RN 168635-71-0 HCAPLUS
CN Thymidine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P,2'-dideoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



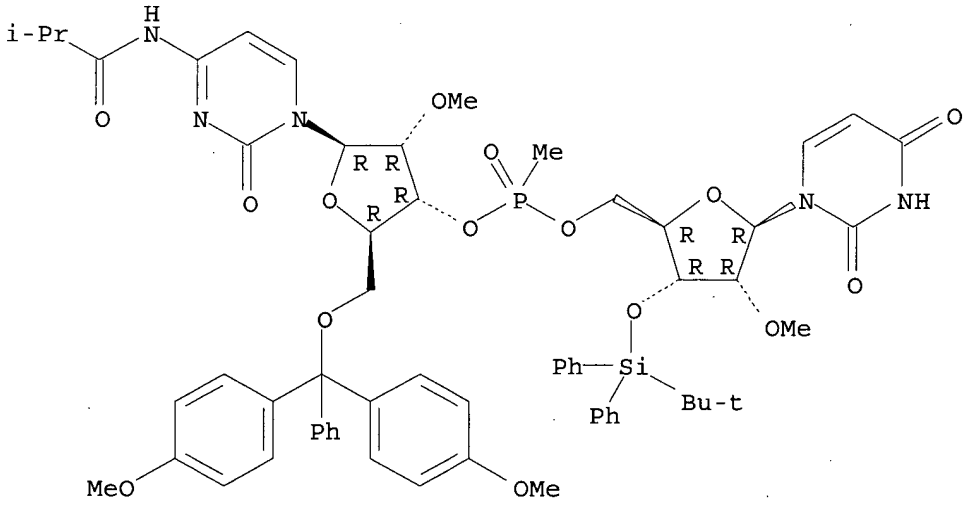
RN 168635-72-1 HCAPLUS
CN Thymidine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P,2'-dideoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-, 3'-[P-methyl-N,N-bis(1-methylethyl)phosphonamidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



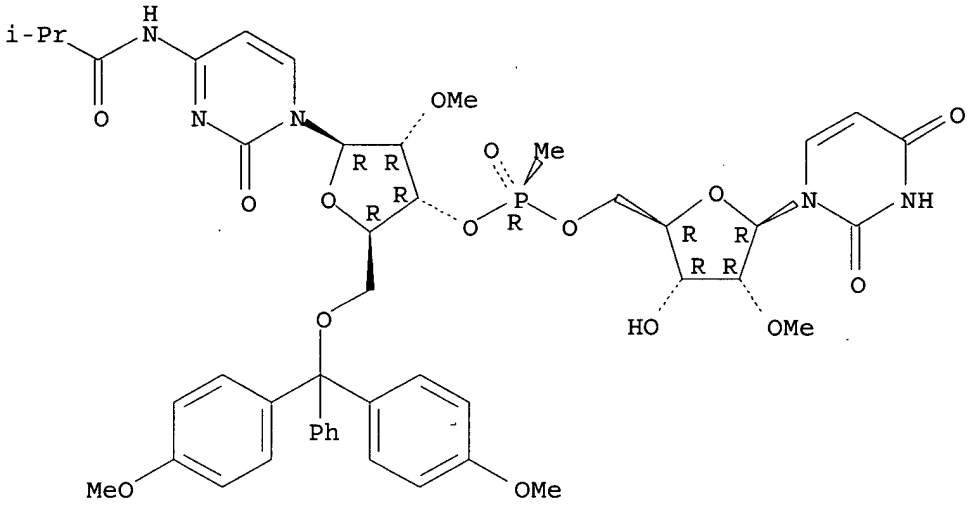
RN 168635-77-6 HCAPLUS
CN Uridine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-2'-O-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-3-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



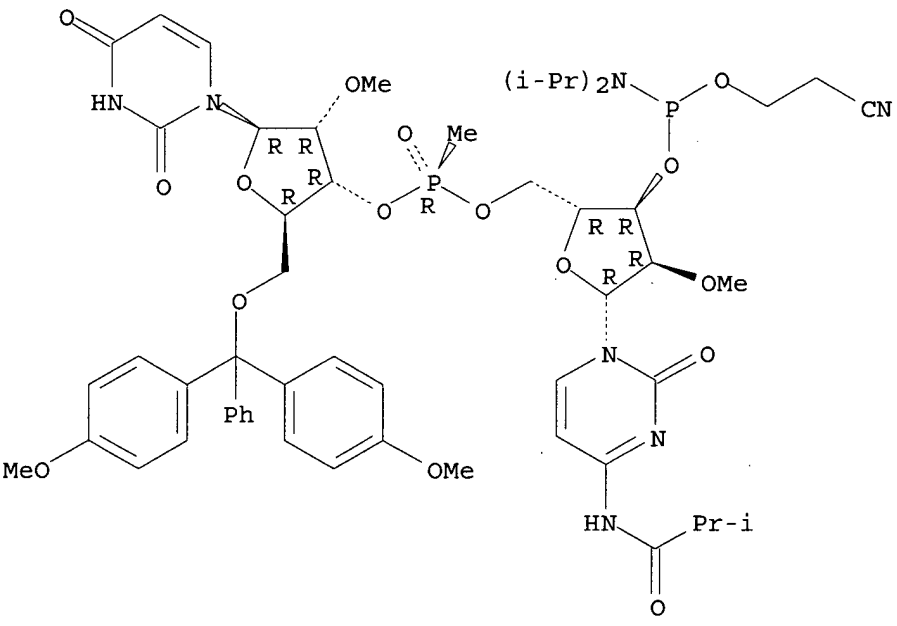
RN 168635-78-7 HCAPLUS
CN Uridine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-2'-O-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



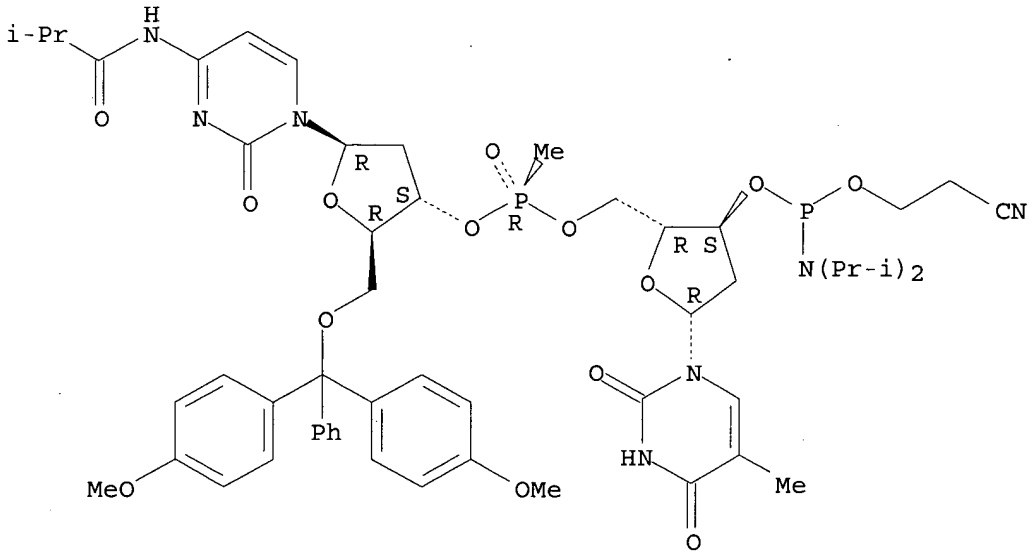
RN 168635-81-2 HCAPLUS
CN Cytidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-2'-O-methyluridylyl-(3'→5')-2'-O-methyl-N-(2-methyl-1-oxopropyl)-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



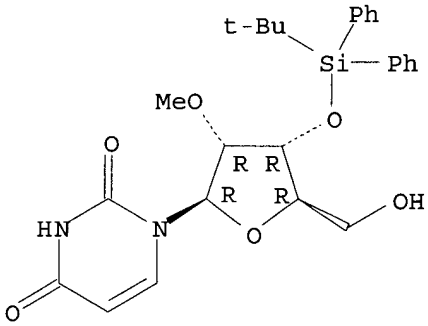
RN 168635-82-3 HCAPLUS
CN Thymidine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P,2'-dideoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



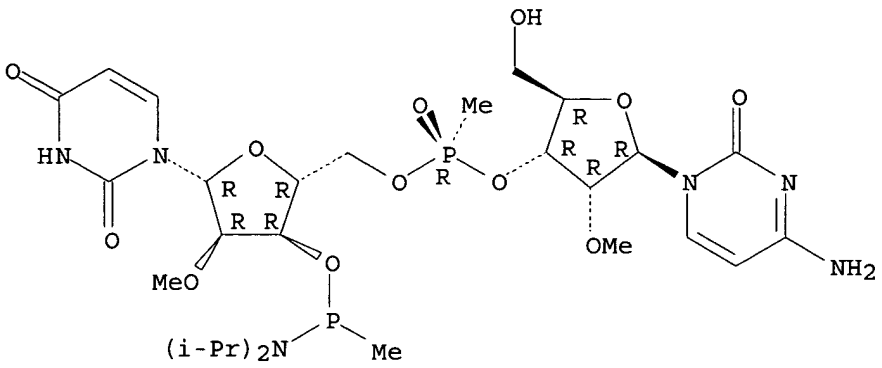
RN 168635-83-4 HCAPLUS
CN Uridine, 3'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



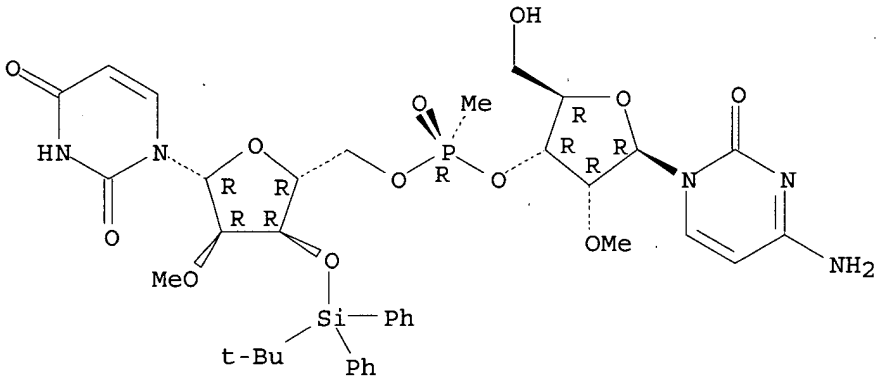
RN 168635-84-5 HCAPLUS
CN Uridine, (R)-P-deoxy-P-methyl-2'-O-methylcytidylyl-(3'→5')-2'-O-methyl-, 3'-[P-methyl-N,N-bis(1-methylethyl)phosphonamidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



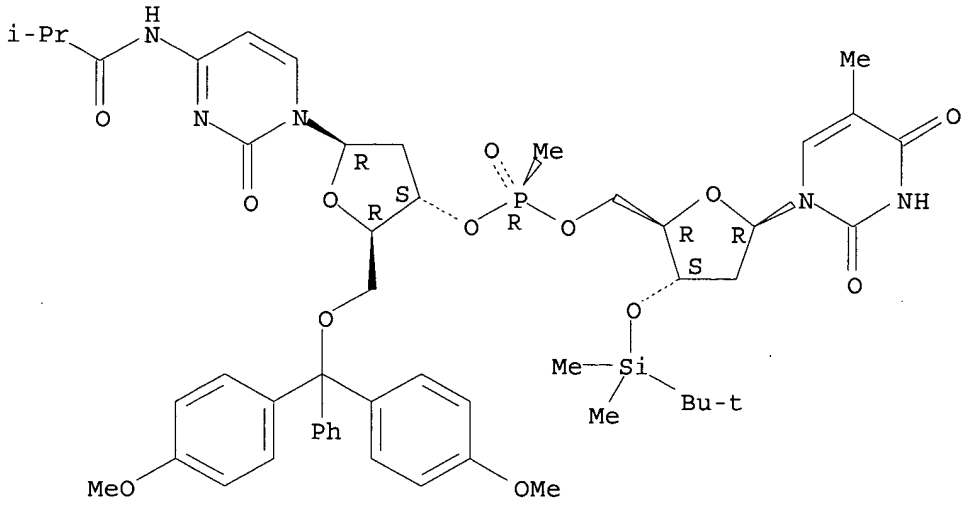
RN 168752-52-1 HCAPLUS
CN Uridine, (R)-P-deoxy-P-methyl-2'-O-methylcytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



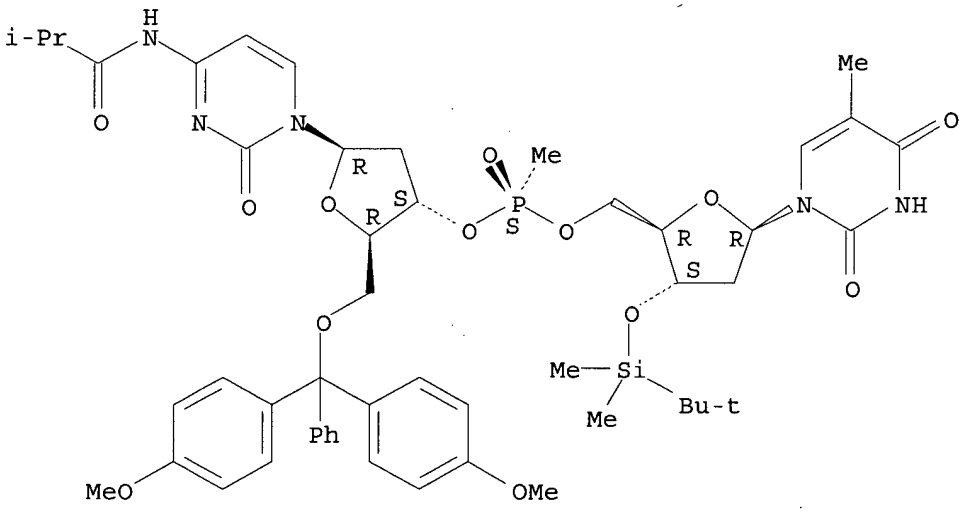
RN 168752-53-2 HCAPLUS
CN Thymidine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



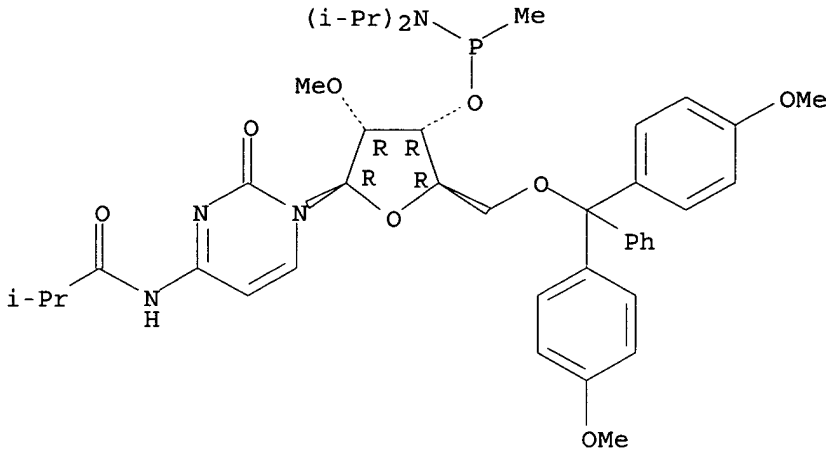
RN 168752-54-3 HCAPLUS
CN Thymidine, [P(S)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 168752-56-5 HCAPLUS
CN Cytidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyl-N-(2-methyl-1-oxopropyl)-, 3'-[P-methyl-N,N-bis(1-methylethyl)phosphonamidate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 24 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:846611 HCAPLUS
DOCUMENT NUMBER: 123:248526
TITLE: **Oligonucleotides** with phosphonate **internucleosidyl** linkages of undefined **chirality** mixed with non-phosphonate **internucleosidyl** linkages: their preparation and use in preventing formation or translation of RNA
INVENTOR(S): Dwyer, Brian Patrick; Arnold, Lyle John, Jr.; Reynolds, Mark Alan
PATENT ASSIGNEE(S): Genta Inc., USA
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9513833	A1	19950526	WO 1994-US13386		19941116
W: AU, CA, JP, KR, NZ					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
CA 2176498	AA	19950526	CA 1994-2176498		19941116
AU 9512915	A1	19950606	AU 1995-12915		19941116
AU 687492	B2	19980226			
EP 735899	A1	19961009	EP 1995-904097		19941116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
JP 09505306	T2	19970527	JP 1994-514645		19941116
IL 128658	A1	20030312	IL 1994-128658		19941116
US 6060456	A	20000509	US 1997-960111		19971027
PRIORITY APPLN. INFO.:			US 1993-154014	A	19931116
			US 1994-233778	A	19940426
			US 1994-238177	A	19940504
			US 1993-154013	A	19931116
			IL 1994-111660	A3	19941116
			WO 1994-US13386	W	19941116
			US 1995-481637	B1	19950607

OTHER SOURCE(S): MARPAT 123:248526
ED Entered STN: 11 Oct 1995

AB Oligomers having phosphonate internucleosidyl linkages mixed with non-phosphonate internucleosidyl linkages which hybridize to RNA target sequences and methods for their preparation are provided. Dinucleotide synthons containing racemic methylphosphonate linkages and oligonucleotides containing these synthons were prepared Relative to oligonucleotides having all phosphodiester linkages, the chimeric oligonucleotides displayed greater resistance to nuclease digestion, to degradation in bacterial and mammalian cell lysates and in vivo.

IC ICM A61K048-00
ICS C07H021-02; C07H021-04

CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 33

IT **Transcription, genetic**
Translation, genetic
(preparation of chimeric racemic phosphonate/nonphosphonate-linked oligonucleotides and their use in preventing formation or translation of RNA)

IT **Nucleotides, biological studies**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**oligo**-, phosphonate-linked; preparation of chimeric racemic phosphonate/nonphosphonate-linked oligonucleotides and their use in preventing formation or translation of RNA)

IT **2140-72-9 40733-27-5** 51747-24-1 58479-61-1
89992-70-1 **103285-22-9** 114745-26-5 **128192-22-3**
153809-39-3 168635-73-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of chimeric racemic phosphonate/nonphosphonate-linked oligonucleotides and their use in preventing formation or translation of RNA)

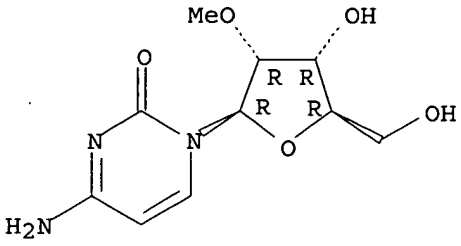
IT **168635-65-2P 168635-66-3P 168635-67-4P**
168635-70-9P 168635-74-3P 168635-75-4P 168635-76-5P
168635-77-6P 168635-78-7P 168635-79-8P
168635-83-4P 168752-56-5P 168959-63-5P
168959-64-6P 168959-65-7P 168959-66-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of chimeric racemic phosphonate/nonphosphonate-linked oligonucleotides and their use in preventing formation or translation of RNA)

IT **168752-53-2P 168752-54-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of chimeric racemic phosphonate/nonphosphonate-linked oligonucleotides and their use in preventing formation or translation of RNA)

IT **2140-72-9 40733-27-5 103285-22-9**
128192-22-3 153809-39-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of chimeric racemic phosphonate/nonphosphonate-linked oligonucleotides and their use in preventing formation or translation of RNA)

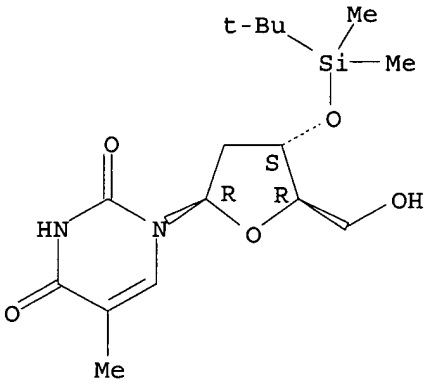
RN 2140-72-9 HCAPLUS
CN Cytidine, 2'-O-methyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



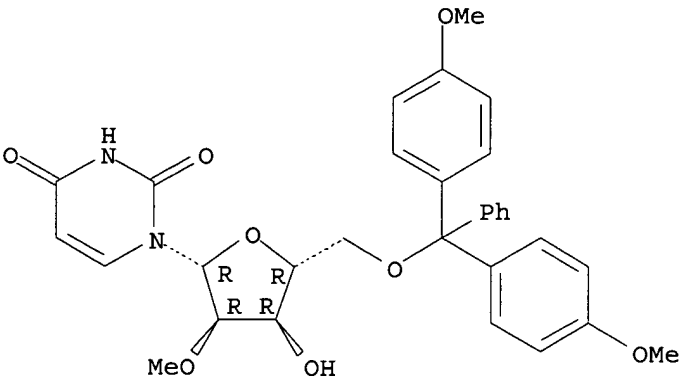
RN 40733-27-5 HCAPLUS
CN Thymidine, 3'-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



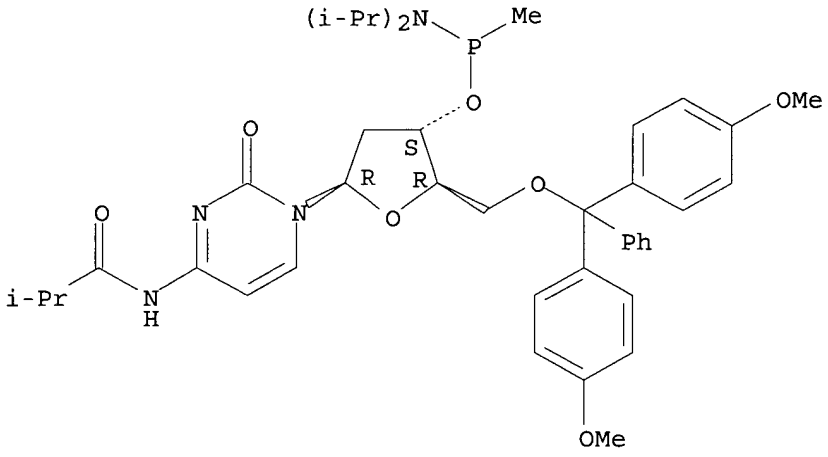
RN 103285-22-9 HCAPLUS
CN Uridine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



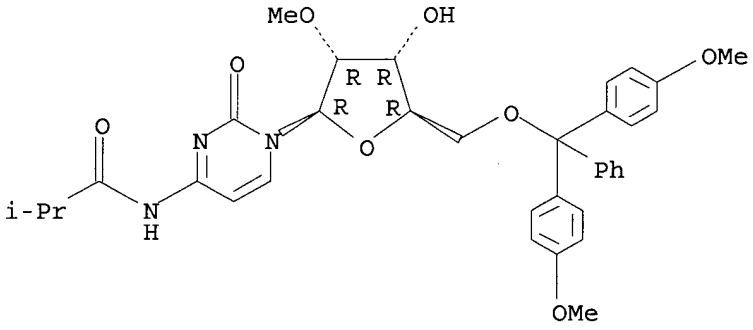
RN 128192-22-3 HCAPLUS
CN Cytidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-N-(2-methyl-1-oxopropyl)-, 3'-[P-methyl-N,N-bis(1-methylethyl)phosphonamidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



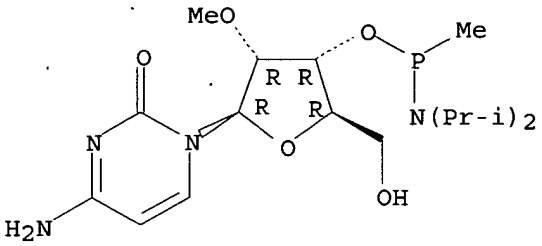
RN 153809-39-3 HCAPLUS
CN Cytidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyl-N-(2-methyl-1-oxopropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



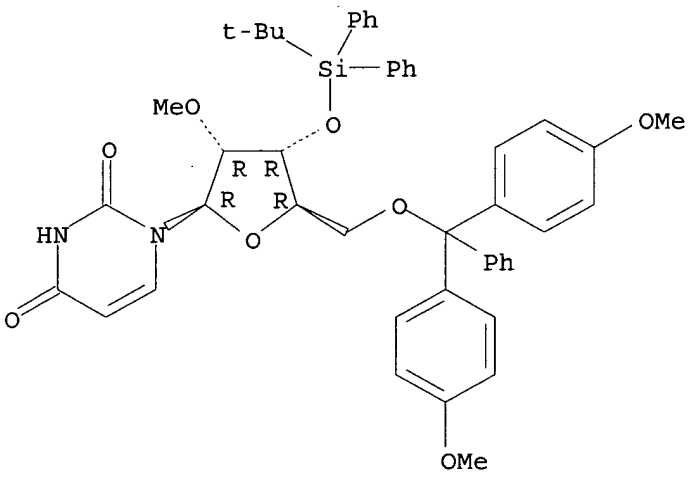
IT **168635-65-2P 168635-66-3P 168635-67-4P**
168635-70-9P 168635-77-6P 168635-78-7P
168635-83-4P 168752-56-5P 168959-63-5P
168959-64-6P 168959-65-7P 168959-66-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of chimeric racemic phosphonate/nonphosphonate-linked oligonucleotides and their use in preventing formation or translation of RNA)
RN 168635-65-2 HCAPLUS
CN Cytidine, 2'-O-methyl-, 3'-[P-methyl-N,N-bis(1-methylethyl)phosphonamidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



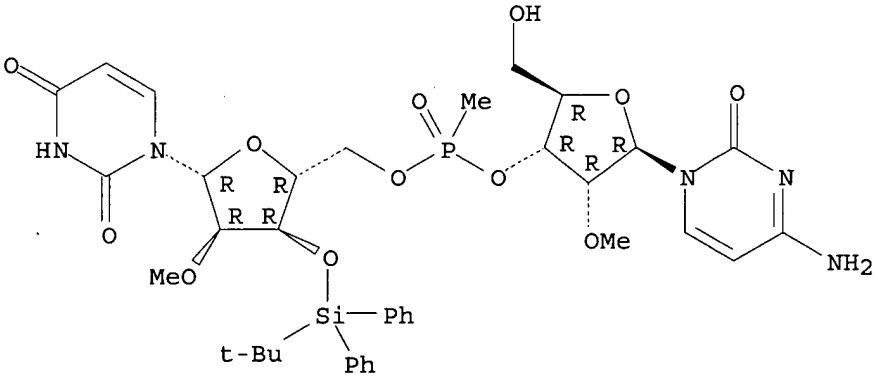
RN 168635-66-3 HCAPLUS
CN Uridine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-3'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 168635-67-4 HCAPLUS
CN Uridine, P-deoxy-P-methyl-2'-O-methylcytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

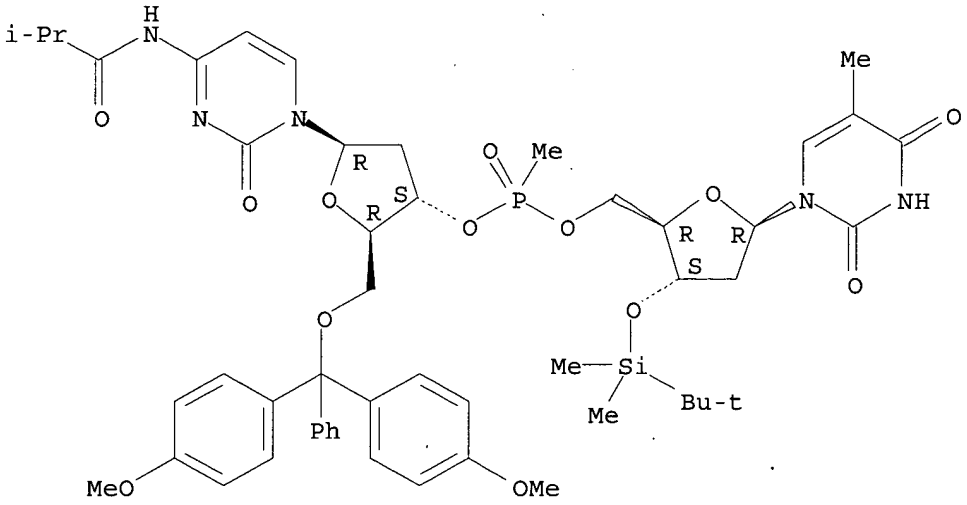
Absolute stereochemistry.



RN 168635-70-9 HCAPLUS

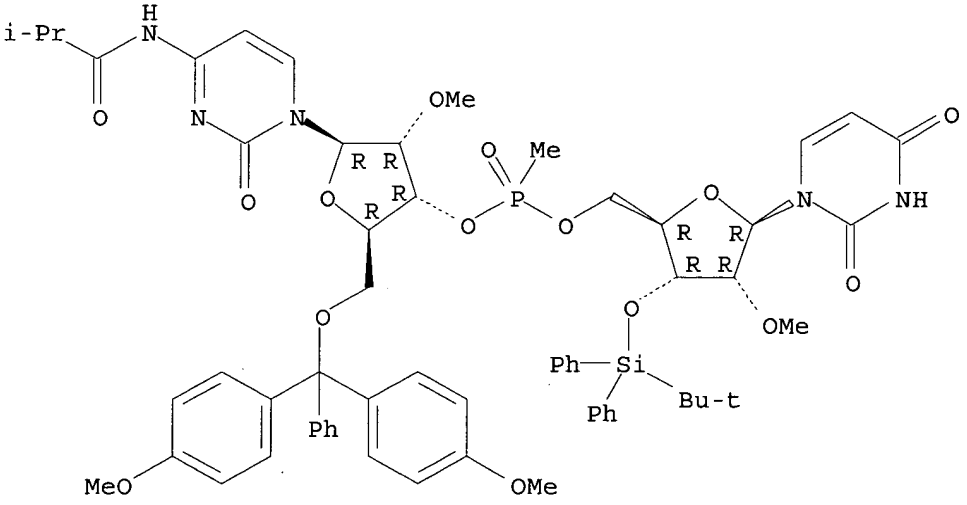
CN Thymidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P,2'-dideoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



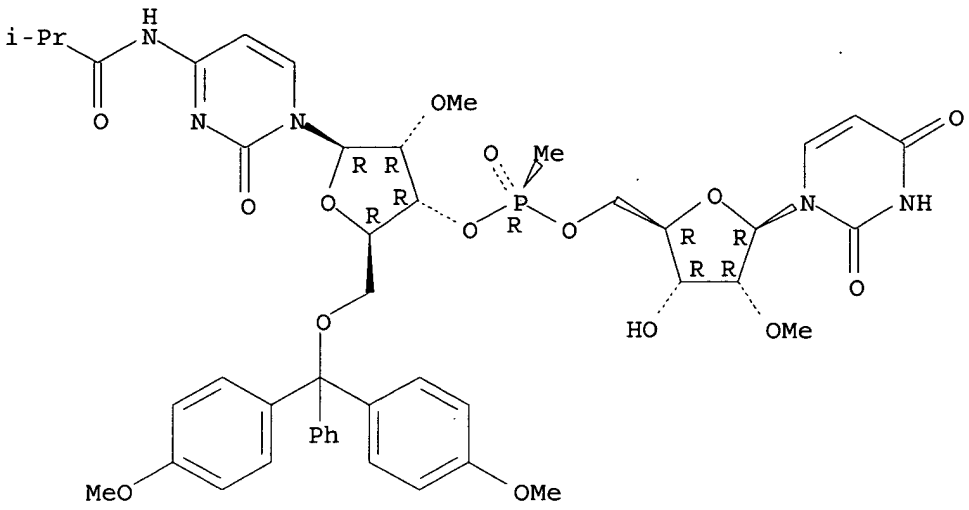
RN 168635-77-6 HCAPLUS
CN Uridine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-2'-O-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-3-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



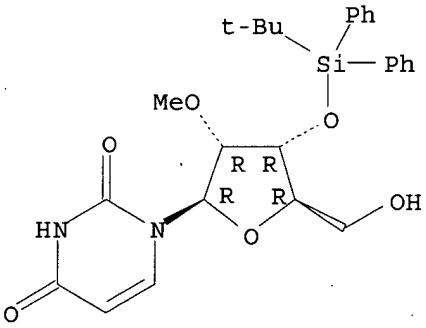
RN 168635-78-7 HCAPLUS
CN Uridine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-2'-O-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



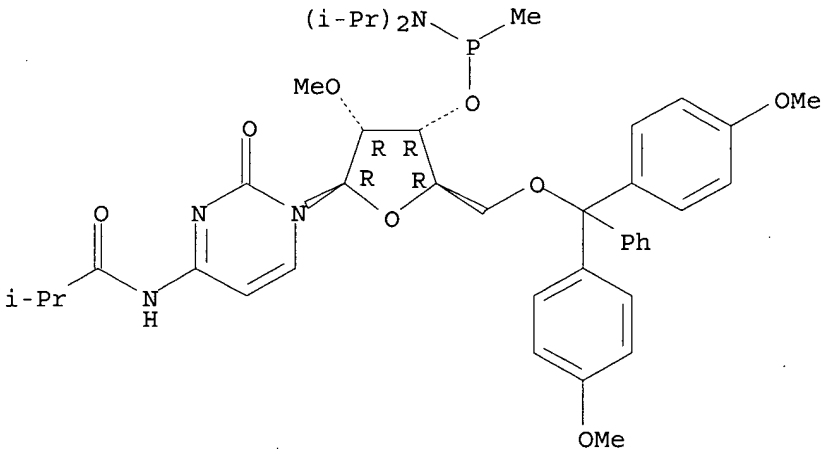
RN 168635-83-4 HCAPLUS
CN Uridine, 3'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



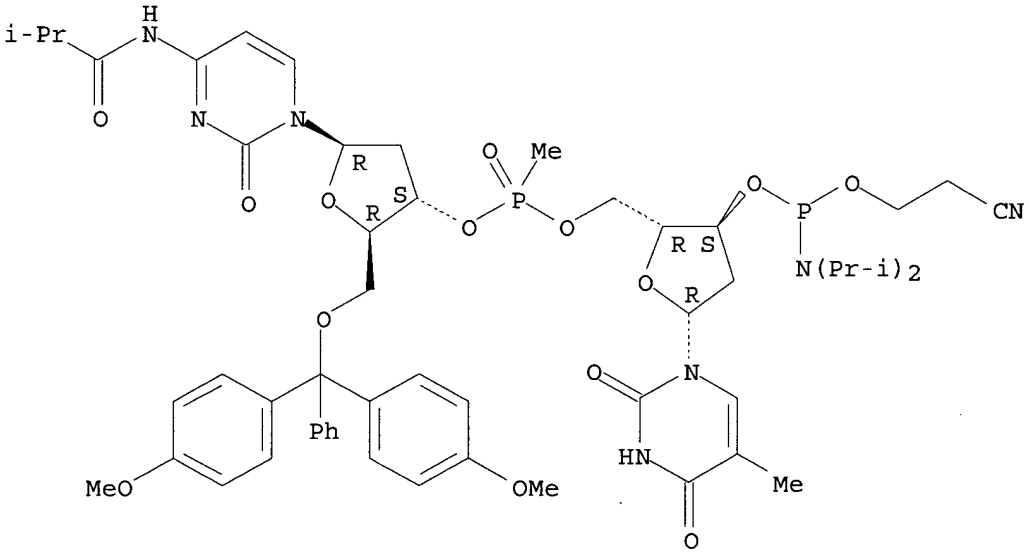
RN 168752-56-5 HCAPLUS
CN Cytidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyl-N-(2-methyl-1-oxopropyl)-, 3'-[P-methyl-N,N-bis(1-methylethyl)phosphonamidate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



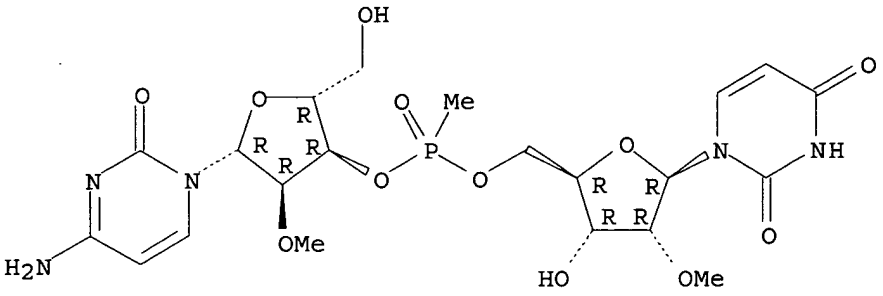
RN 168959-63-5 HCAPLUS
CN Thymidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P,2'-dideoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



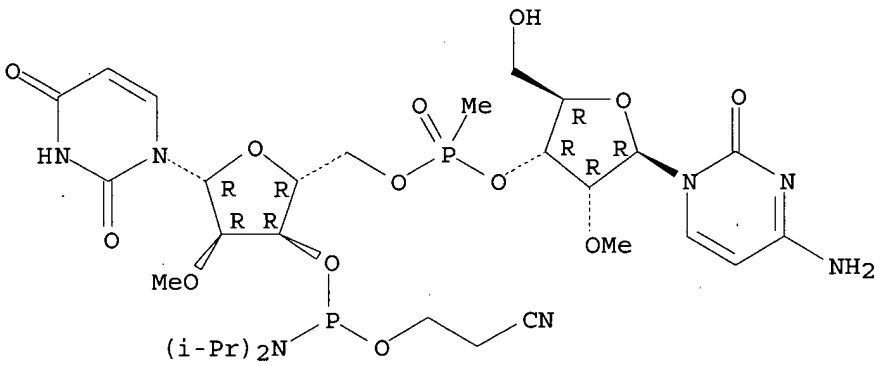
RN 168959-64-6 HCAPLUS
CN Uridine, P-deoxy-P-methyl-2'-O-methylcytidylyl-(3'→5')-2'-O-methyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



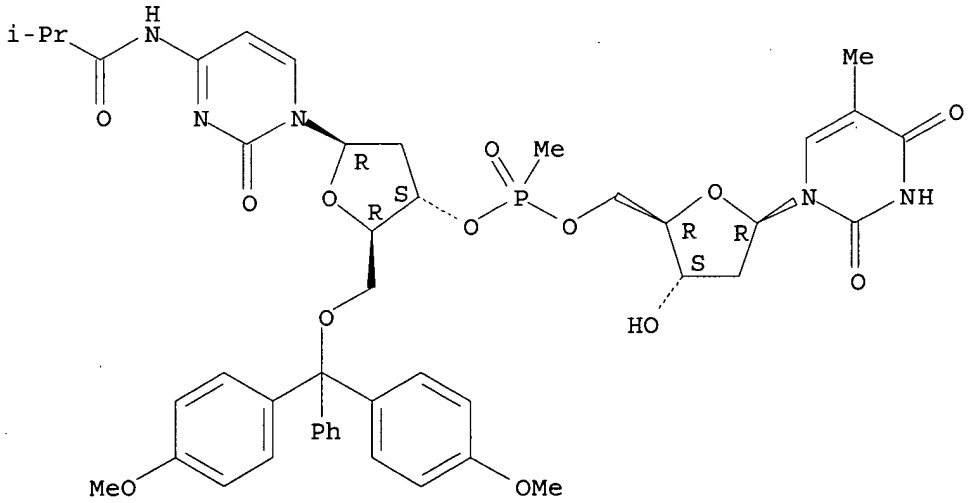
RN 168959-65-7 HCAPLUS
CN Uridine, P-deoxy-P-methyl-2'-O-methylcytidylyl-(3'→5')-2'-O-methyl-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 168959-66-8 HCAPLUS
CN Thymidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P,2'-dideoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')- (9CI) (CA INDEX NAME)

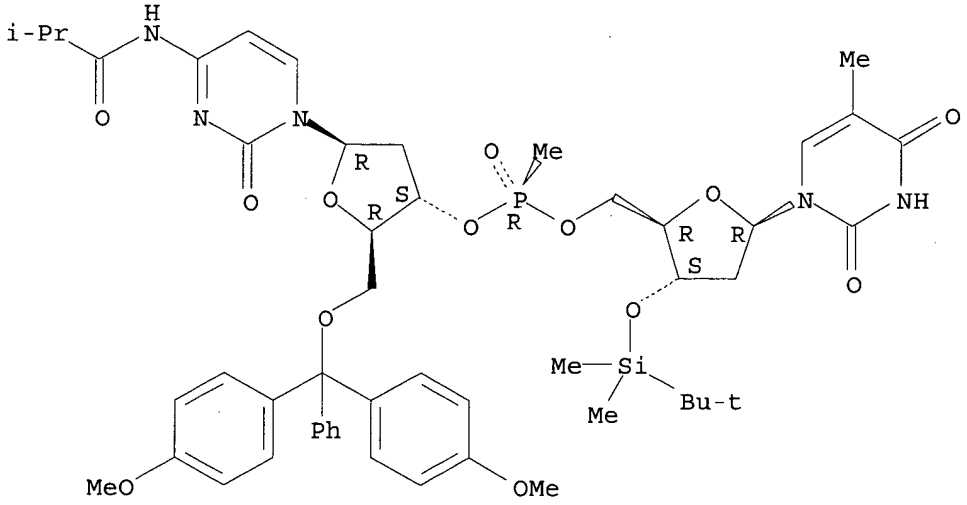
Absolute stereochemistry.



IT **168752-53-2P 168752-54-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of chimeric racemic phosphonate/nonphosphonate-linked oligonucleotides and their use in preventing formation or translation of RNA)

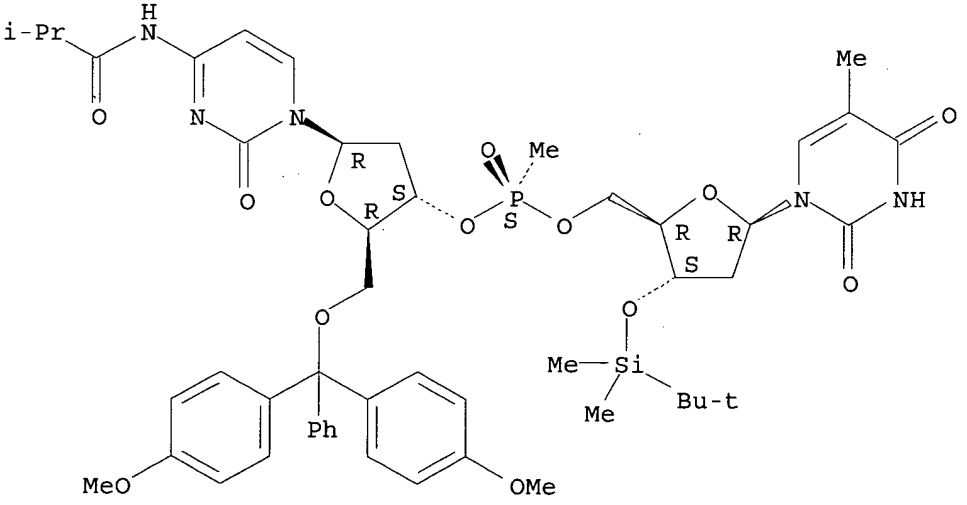
RN 168752-53-2 HCAPLUS
CN Thymidine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



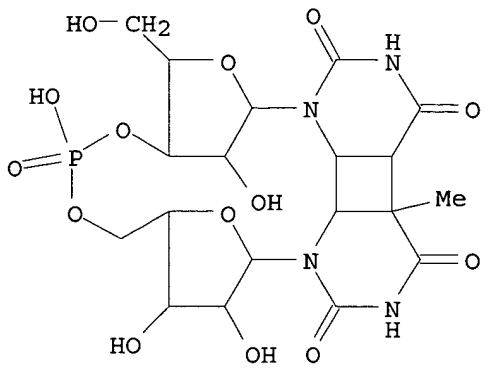
RN 168752-54-3 HCAPLUS
CN Thymidine, [P(S)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

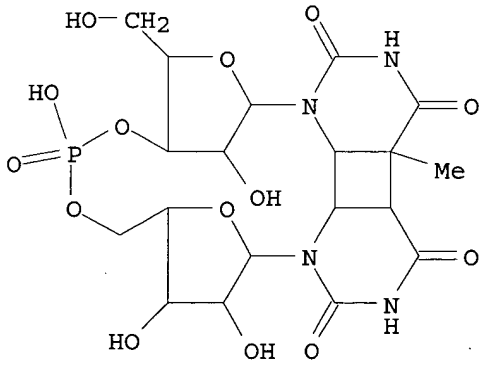


L89 ANSWER 25 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:647730 HCAPLUS
DOCUMENT NUMBER: 123:286503
TITLE: Solution structure of a nucleic acid photoproduct of deoxyfluorouridylyl-(3'-5')-thymidine monophosphate (d-FpT) determined by NMR and restrained molecular dynamics: structural comparison of two sequence isomer photoadducts (d-U5p5T and d-T5p5U)
AUTHOR(S): Kim, Jong-Ki; Soni, Sunil-Datta; Arakali, Aruna V.; Wallace, John C.; Alderfer, James L.
CORPORATE SOURCE: Biophys. Dep., Roswell Park Cancer Inst., Buffalo, NY, 14263, USA
SOURCE: Nucleic Acids Research (1995), 23(10), 1810-15
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 30 Jun 1995
AB Acetone-sensitized irradiation using UV-B (sun lamp, λmax = 313 nm) of deoxyfluorouridylyl-(3'-5')-thymidine monophosphate (d-FpT, F = fluorouracil), produces two major photoproducts, the cis-syn cyclobutane-type photodimer and a defluorinated (5-5) photoadduct, d-U5p5T. Product distribution is dependent on the pH of the irradiation solution, as was the case of irradiated d-TpF. At high pH (8-10) the (5-5) photoadduct is the major photoproduct. Irradiation of d-FpT shows a much faster photodegrdn. rate than the sequence isomer d-TpF. Multinuclear NMR expts. establish the formation of (5-5) covalent bonding between the C5 (d-U5p-, where the fluorine had been) and the C5 (-p5T) and the C6 (-p5T) acquires an OH group. NOE interproton distances and dihedral angles derived from J coupling anal. are constrained to refine model structures of d-U5p5T in restrained mol. dynamics calcualtions. The resultant structures obtained show 5S-6S as the most probable **chiralities** of the C5 and C6 atoms of the thymine, which is the opposite **chirality** to the corresponding atoms in the sequence isomer d-T5p5U. The orientation of the C5 substituents (-p5T fragment), the CH3 and the uracil are pseudo-axial and pseudo-equatorial resp. Glycosidic angles are in the anti regions for both the d-U5p- and -p5T residues. Averaged backbone conformations of the two photoadducts, d-U5p5T and d-T5p5U, are similar, although the overall structure of d-U5p5T appears much more flexible than that of d-T5p5U. In particular, the sugar conformations of the 5'-end residues show a remarkable difference in flexibility.
CC 33-10 (Carbohydrates)
IT **Nucleotides, preparation**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(**oligo-**, **deoxyribo-**, solution structure of a nucleic acid photoproduct of deoxyfluorouridylylthymidine monophosphate determined by NMR and restrained mol. dynamics)
IT 1546-25-4 13276-67-0 **169558-30-9 169558-31-0**
RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
(solution structure of a nucleic acid photoproduct of deoxyfluorouridylylthymidine monophosphate determined by NMR and restrained mol. dynamics)
IT **169558-30-9 169558-31-0**
RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
(solution structure of a nucleic acid photoproduct of deoxyfluorouridylylthymidine monophosphate determined by NMR and restrained mol. dynamics)
RN 169558-30-9 HCAPLUS

CN 9,12-Epoxy-1,4-methano-1H,6H,8H-2,5,7-trioxa-12a,14,17,18a-tetraaza-6-phosphacyclohexadeca[def]biphenylene-13,15,16,18(14H,17H)-tetrone, decahydro-6,10,11,20-tetrahydroxy-3-(hydroxymethyl)-15a-methyl-, 6-oxide, [1R-(1R*,3R*,4S*,9R*,10S*,11R*,12R*,15aS*,15bR*,18bR*,18cS*,20R*)]- (9CI) (CA INDEX NAME)



RN 169558-31-0 HCAPLUS
CN 9,12-Epoxy-1,4-methano-1H,6H,8H-2,5,7-trioxa-12a,14,17,18a-tetraaza-6-phosphacyclohexadeca[def]biphenylene-13,15,16,18(14H,17H)-tetrone, decahydro-6,10,11,20-tetrahydroxy-3-(hydroxymethyl)-15b-methyl-, 6-oxide, [1R-(1R*,3R*,4S*,9R*,10S*,11R*,12R*,15aS*,15bR*,18bR*,18cS*,20R*)]- (9CI) (CA INDEX NAME)



L89 ANSWER 26 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:209840 HCAPLUS
DOCUMENT NUMBER: 116:209840
TITLE: Computer modeling of gibberellin-DNA binding
AUTHOR(S): Witham, Francis H.; Hendry, Lawrence B.
CORPORATE SOURCE: Dep. Hortic., Pennsylvania State Univ., University Park, PA, 16802, USA
SOURCE: Journal of Theoretical Biology (1992), 155(1), 55-67
CODEN: JTBIAP; ISSN: 0022-5193
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 31 May 1992
AB Computer modeling and mol. mechanics performed on the intercalation complexes of selected gibberellins or biosynthetic precursors with DNA

dinucleotides revealed that under appropriate conditions the ligands insert (intercalate) between the base-paired double-stranded **dinucleotide**, 5'-dTdA-3'. Stabilization of the double-stranded **dinucleotide** after docking of a gibberellin between base pairs is inferred by the sum neg. energy of hydrogen bonding and van der Waals contacts and the entropic changes which accompany the formation of each ligand-**dinucleotide** complex. In addition, the interactions of the gibberellins and **dinucleotides**, with the gibberellic acid-**dinucleotide** complex serving as the prototype, show optimum geometry and stereochem. hydrogen bonding recognition which are dependent upon the complementary **chirality** and stereochem. of the individual components. Whether or not the gibberellins directly influence the uncoiling of DNA or **gene expression** at the **transcriptional** level via an intercalation mechanism is a matter of conjecture, albeit one that warrants intensive investigation.

CC 6-2 (General Biochemistry)
Section cross-reference(s): 11

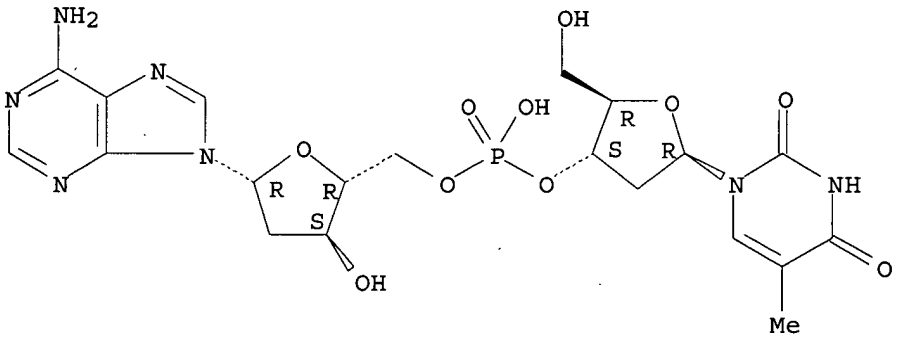
IT **Nucleotides, polymers**
RL: BIOL (Biological study)
(**di**-, gibberellins intercalation by, computer modeling of)

IT **19192-40-6**
RL: PRP (Properties)
(gibberellins intercalation by, computer modeling of)

IT **19192-40-6**
RL: PRP (Properties)
(gibberellins intercalation by, computer modeling of)

RN 19192-40-6 HCAPLUS
CN Adenosine, thymidylyl-(3'→5')-2'-deoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d ibib ed ab hitstr hitind 27
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, TOXCENTER, USPATFULL, WPIX, BIOSIS, CANCERLIT, BIOTECHNO, BIOTECHDS, SCISEARCH' - CONTINUE? (Y)/N:y

'HITSTR' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid in at least one of the files. Refer to file specific help messages or the STNGUIDE file for information on formats available in individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):ibib ed ab hitind

L89 ANSWER 27 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:118630 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA141101526730
TITLE: NMR structure of the DNA decamer duplex containing double T·G mismatches of cis-syn cyclobutane pyrimidine dimer: implications for DNA damage recognition by the XPC-hHR23B complex
AUTHOR(S): Lee, Joon-Hwa; Park, Chin-Ju; Shin, Jae-Sun; Ikegami, Takahisa; Akutsu, Hideo; Choi, Byong-Seok
CORPORATE SOURCE: Department of Chemistry and National Creative Research Initiative Center, Korea Advanced Institute of Science and Technology, Daejon, Yuseong-gu, 305-701, S. Korea.
SOURCE: Nucleic Acids Research, (2004) Vol. 32, No. 8, pp. 2474-2481.
CODEN: NARHAD. ISSN: 0305-1048.
COUNTRY: KOREA, REPUBLIC OF
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2004:402214
LANGUAGE: English
ENTRY DATE: Entered STN: 20040525
Last Updated on STN: 20041221
ED Entered STN: 20040525
Last Updated on STN: 20041221
AB The cis-syn cyclobutane pyrimidine dimer (CPD) is a cytotoxic, mutagenic and carcinogenic DNA photoproduct and is repaired by the **nucleotide** excision repair (NER) pathway in mammalian cells. The XPC-hHR23B complex as the initiator of global genomic NER binds to sites of certain kinds of DNA damage. Although CPDs are rarely recognized by the XPC-hHR23B complex, the presence of mismatched bases opposite a CPD significantly increased the binding affinity of the XPC-hHR23B complex to the CPD. In order to decipher the properties of the DNA structures that determine the binding affinity for XPC-hHR23B to DNA, we carried out structural analyses of the various types of CPDs by NMR spectroscopy. The DNA duplex which contains a single 3' T·G wobble pair in a CPD (CPD/GA duplex) induces little conformational distortion. However, severe distortion of the helical conformation occurs when a CPD contains double T·G wobble pairs (CPD/GG duplex) even though the T residues of the CPD form stable hydrogen bonds with the opposite G residues. The helical bending angle of the CPD/GG duplex was larger than those of the CPD/GA duplex and properly matched CPD/AA duplex. The fluctuation of the backbone conformation and significant changes in the widths of the major and minor grooves at the double T·G wobble paired site were also observed in the CPD/GG duplex. These structural features were also found in a duplex that contains the (6-4) adduct, which is efficiently recognized by the XPC-hHR23B complex. Thus, we suggest that the unique structural features of the DNA double helix (i.e., helical bending, flexible backbone conformation, and significant changes of the major and/or minor grooves) might be important factors in determining the binding affinity of the XPC-hHR23B complex to DNA.
CC 6-2
ST Miscellaneous Descriptors
conformation DNA thymine guanine mismatch cyclobutane pyrimidine dimer
RN 65-71-4 (Thymine)
73-40-5 (Guanine)
RN **4472-37-1**; 730130-31-1; 730130-32-2; 730130-33-3

=> d ibib ed ab hitind 28-54
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, TOXCENTER, USPATFULL, WPIX, BIOSIS, CANCERLIT, BIOTECHNO, BIOTECHDS, SCISEARCH' - CONTINUE? (Y)/N:y

L89 ANSWER 28 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:275122 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA13924360547N
TITLE: Independent Generation of 5-(2'-Deoxycytidinyl)methyl Radical and the Formation of a Novel Cross-Link Lesion between 5-Methylcytosine and Guanine
AUTHOR(S): Zhang, Qibin; Wang, Yinsheng
CORPORATE SOURCE: Department of Chemistry, University of California at Riverside, Riverside, CA, 92521-0403, USA.
SOURCE: Journal of the American Chemical Society, (2003) Vol. 125, No. 42, pp. 12795-12802.
CODEN: JACSAT. ISSN: 0002-7863.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2003:738572
LANGUAGE: English
ENTRY DATE: Entered STN: 20031117
Last Updated on STN: 20040622
ED Entered STN: 20031117
Last Updated on STN: 20040622
AB Reactive oxygen species (ROS) can damage DNA. Although a number of single **nucleobase** lesions induced by ROS have been structurally characterized, only a few intrastrand cross-link lesions have been identified and characterized, and all of them involve adjacent thymine and guanine or adenine. In mammalian cells, the cytosines at CpG sites are methylated. On the basis of the similar reactivity of 5-methylcytosine and thymine toward hydroxyl radical and the similar orientation of adjacent thymine guanine (TG) and 5-methylcytosine guanine (mCG) in B-DNA, we predict that the cross-link lesion, which was identified in TG and has a covalent bond formed between the 5-Me carbon atom of T and the C8 carbon atom of G, should also form at mCG site. Here, we report for the first time the independent generation of 5-(2'-deoxycytidinyl)methyl radical, and our results demonstrate that this radical can give rise to the predicted novel intrastrand cross-link lesion in **dinucleoside** monophosphates d(mCG) and d(GmC). Furthermore, we show that the cross-link lesion can also form in d(mCG) from γ irradiation under anaerobic conditions.
CC 6-2
ST Miscellaneous Descriptors
guanine methylcytosine crosslinking DNA deoxycytidinylmethyl radical
RN 7782-44-7Q (Oxygen, reactive species)
73-40-5 (Guanine)
554-01-8 (5-Methylcytosine)
108-24-7 (Acetic anhydride)
108-98-5 (Benzenethiol)
288-88-0 (1H-1,2,4-Triazole)
RN 39071-65-3; **622402-68-0**; **622402-69-1**; 951-78-0; 40615-36-9; 68892-42-2; 89992-70-1; 272116-46-8; 272116-47-9; 272116-56-0; 622402-60-2; 622402-61-3; 622402-63-5; 622402-64-6; 622402-65-7; 622402-66-8; 693221-79-3; 622402-62-4; 622402-67-9

L89 ANSWER 29 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:226737 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA13925377179S
TITLE: Sequence context-dependent replication of DNA templates containing UV-induced lesions by human DNA polymerase ι
AUTHOR(S): Vaisman, Alexandra; Frank, Ekaterina G.; Iwai, Shigenori; Ohashi, Eiji; Ohmori, Haruo; Hanaoka, Fumio; Woodgate, Roger
CORPORATE SOURCE: National Institute of Child Health and Human Development, Laboratory of Genomic Integrity, Repair and Mutagenesis, Section on DNA Replication, National Institutes of Health, Bethesda, MD, 20892-2725, USA.
SOURCE: DNA Repair, (2003) Vol. 2, No. 9, pp. 991-1006. CODEN: DRNEAR. ISSN: 1568-7864.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2003:705263
LANGUAGE: English
ENTRY DATE: Entered STN: 20030916
Last Updated on STN: 20031216

ED Entered STN: 20030916
Last Updated on STN: 20031216

AB Humans possess four Y-family polymerases: pols η, ι, κ and the Rev1 protein. The pivotal role that polη plays in protecting us from UV-induced skin cancers is unquestioned given that mutations in the POLH gene (encoding polη), lead to the sunlight-sensitive and cancer-prone xeroderma pigmentosum variant phenotype. The roles that pols ι, κ and Rev1 play in the tolerance of UV-induced DNA damage is, however, much less clear. For example, in vitro studies in which the ability of polι to bypass UV-induced cyclobutane pyrimidine dimers (CPDs) or 6-4 pyrimidine-pyrimidone (6-4PP) lesions has been assayed, are somewhat varied with results ranging from limited misinsertion opposite CPDs to complete lesion bypass. We have tested the hypothesis that such discrepancies might have arisen from different assay conditions and local sequence contexts surrounding each UV-photoproduct and find that polι can facilitate significant levels of unassisted highly error-prone bypass of a T-T CPD, particularly when the lesion is located in a 3'-A[T-T]A-5' template sequence context and the reaction buffer contains no KCl. When encountering a T-T 6-4PP dimer under the same assay conditions, polι efficiently and accurately inserts the correct base, A, opposite the 3'T of the 6-4PP by factors of .apprx.102 over the incorporation of incorrect **nucleotides**, while incorporation opposite the 5'T is highly mutagenic. Polκ has been proposed to function in the bypass of UV-induced lesions by helping extend primers terminated opposite CPDs. However, we find no evidence that the combined actions of polι and polκ result in a significant increase in bypass of T-T CPDs when compared to polι alone. Our data suggest that under certain conditions and sequence contexts, polι can bypass T-T CPDs unassisted and can efficiently incorporate one or more bases opposite a T-T 6-4PP. Such biochem. activities may, therefore, be of biol. significance especially in XP-V cells lacking the primary T-T CPD bypassing enzyme, polη.

CC 7-4

ST Miscellaneous Descriptors
DNA replication UV lesion human polymerase iota sequence KCl; pyrimidine dimer error prone bypass human DNA polymerase iota

RN 243664-63-3 (DNA polymerase ι)

RN **4472-37-1; 100850-36-0**

L89 ANSWER 30 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:279528 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA13726385074C
TITLE: Preparation of acyclic **nucleosides** as antiviral and antitumor agents
AUTHOR(S): Kumar, Rakesh; Agrawal, Babita; Tyrrell, D. Lorne J.
PATENT INFORMATION: WO 2002094844 A2 28 Nov 2002
SOURCE: (2002) PCT Int. Appl., 140 pp.
CODEN: PIXXD2.
COUNTRY: CANADA
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2002:906253
LANGUAGE: English
ENTRY DATE: Entered STN: 20021210
Last Updated on STN: 20050215

ED Entered STN: 20021210
Last Updated on STN: 20050215

AB Disclosed are **nucleosides** I wherein X is O, S, N:CHNMe2, OH, alkoxy, thio, acyloxy, amino, aminoacyl, aminoacyloxy; X1 is O, S; Y is O, S, NH, NAc; R is H, alkyl, acyl, acylamino, alkylcarboxyl; R1 is is H, halogen, alkyl, alkoxy, alkoxy, hydroxyl, amino, substituted amino, aminoacyl, thiol, thioalkoxy, carboxy, alkylcarboxyl, acylamino, acyl, aryl, alkaryl, nitro, cyano, thiocyano, azido, -CH2OCHO, formyl; R2 is H, OH, OAc, OMe, halogen; Z-Z1 is CR4R5-CR6R7 wherein R4-R7 are independently H, OH, halogen, CN, CH2OH, Co2H, alkyl substituted carboxy, NH2, CH2NH2, CH2CO2H, thioalkyl, thiol, ONO2, ONH2, CF3, CNS, NHCN, CH2N3, aminoalkyl, CHO, CH=CH, alkoxy, OCH2-aryl, SCH2, OCH2, alkylidene, which are useful in diagnosing and treating viral infections, for example, infections caused by hepatitis B virus (HBV), and herpes viruses including Epstein Barr virus. Thus, 1-[(2-hydroxyethoxy)methyl]-5-(1-azidovinyl)-uracil was prepared and tested for antiviral activity (inhibition of DHBV DNA in duck hepatocytes at 10 μg/mL EC50 = 84.0 μg/mL), antitumor activity (IC50 > 100 μg/mL), and cytotoxicity (CC50 > 100 μg/mL).

CC 33-9

ST Miscellaneous Descriptors
prodrug human hepatitis antiviral prepn acyclic **nucleoside** cytotoxicity antitumor

RN 66-22-8 (Uracil)
128-08-5 (N-Bromosuccinimide)
128-09-6 (N-Chlorosuccinimide)
7790-99-0 (Iodine monochloride)
30516-87-1 (Azt)
172090-26-5 (1-Fluoro-4-hydroxy-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate)

RN 384819-56-1; 384819-57-2; 384819-62-9; 384819-63-0; 397868-94-9; 434306-22-6; 434306-24-8; 90056-98-7; **224797-38-0**; 384819-65-2; 434306-20-4; **475503-15-2**; **475503-16-3**; 475503-32-3; 475503-33-4; 475503-34-5; 475503-35-6; 475503-36-7; 475503-37-8; 475503-38-9; 78692-74-7; 97845-58-4; 434306-34-0; 99305-70-1; 384819-61-8; 434305-94-9; 434305-96-1; 434305-98-3; 434306-00-0; 434306-02-2; 434306-04-4; 434306-06-6; 434306-08-8; 434306-10-2; 434306-12-4; 475503-04-9; 475503-05-0; 475503-06-1; **41308-60-5**; **224797-40-4**; 384819-58-3; 384819-59-4; 384819-60-7; 384819-64-1; 384819-66-3; 434306-16-8; 434306-18-0; 434306-28-2; 434306-30-6; **475503-07-2**; **475503-08-3**; **475503-09-4**; **475503-10-7**; **475503-11-8**; **475503-12-9**; **475503-13-0**; **475503-14-1**; **475503-17-4**; **475503-18-5**; **475503-19-6**; **475503-20-9**;

475503-21-0; 475503-22-1; 475503-23-2;
475503-24-3; 475503-25-4; 475503-26-5;
475503-27-6; 475503-28-7; 475503-29-8;
475503-30-1; 475503-31-2; 475991-46-9

L89 ANSWER 31 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:62303 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA13612178754P
TITLE: DNA repair excision nuclease attacks undamaged DNA: a potential source of spontaneous mutations
AUTHOR(S): Branum, Mark E.; Reardon, Joyce T.; Sancar, Aziz
CORPORATE SOURCE: Department of Biochemistry and Biophysics, University of North Carolina School of Medicine, Chapel Hill, NC, 27599, USA.
SOURCE: Journal of Biological Chemistry, (2001) Vol. 276, No. 27, pp. 25421-25426.
CODEN: JBCHA3. ISSN: 0021-9258.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2001:522430
LANGUAGE: English
ENTRY DATE: Entered STN: 20020313
Last Updated on STN: 20020416
ED Entered STN: 20020313
Last Updated on STN: 20020416
AB **Nucleotide** excision repair is a general repair system that eliminates many dissimilar lesions from DNA. In an effort to understand substrate determinants of this repair system, we tested DNAs with minor backbone modifications using the ultrasensitive excision assay. We found that a phosphorothioate and a methylphosphonate were excised with low efficiency. Surprisingly, we also found that fragments of 23-28 **nucleotides** and of 12-13 **nucleotides** characteristic of human and Escherichia coli excision repair, resp., were removed from undamaged DNA at a significant rate. Considering the relative abundance of undamaged DNA in comparison to damaged DNA in the course of the life of an organism, we conclude that, in general, excision from and resynthesis of undamaged DNA may exceed the excision and resynthesis caused by DNA damage. As resynthesis is invariably associated with mutations, we propose that gratuitous repair may be an important source of spontaneous mutations.
CC 3-4
ST Miscellaneous Descriptors
Escherichia human DNA repair excision nuclease adduct substrate undamaged; mutation spontaneous UvrABC human DNA repair excision nuclease
RN 56-65-5 (Adenosine triphosphate)
52906-91-9 (DNA excision repair nuclease)
81611-73-6 (UvrABC nuclease)
RN 15548-51-3; 73264-62-7; **398474-65-2**

L89 ANSWER 32 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:118411 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA13515211209U
TITLE: **Nucleosides** and **nucleotides.** Part 205. An efficient method for the preparation of 1'α-branched-chain sugar pyrimidine **ribonucleosides** from uridine: the first conversion

of a natural **nucleoside** into 1'-substituted **ribonucleosides**

AUTHOR(S): Kodama, Tetsuya; Shuto, Satoshi; Nomura, Makoto; Matsuda, Akira

CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Hokkaido University, Sapporo, 060-0812, Japan.

SOURCE: Chemistry--A European Journal, (2001) Vol. 7, No. 11, pp. 2332-2340.
CODEN: CEUJED. ISSN: 0947-6539.

COUNTRY: JAPAN

DOCUMENT TYPE: Journal

FILE SEGMENT: CAPLUS

OTHER SOURCE: CAPLUS 2001:436267

LANGUAGE: English

ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20021029

ED Entered STN: 20011116
Last Updated on STN: 20021029

AB 1-[1-C-Phenylseleno-3,5-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-ribopentofuranosyl]uracil was successfully synthesized by enolization of the 3',5'-O-TIPDS-2'-ketouridine, and was subjected to a radical reaction with a vinylsilyl tether-an efficient procedure for preparing 1'α-branched-chain sugar pyrimidine **nucleosides.** Successive treatment of the 3',5'-O-TIPDS-2'-ketouridine with LiHMDS and PhSeCl in THF at < - 70°C gave the desired 1'-phenylseleno products in 85% yield as an anomeric mixture Highly stereoselective reduction at the 2'-carbonyl of the 1'α-product occurred from the β-face by using NaBH4/CeCl3 in MeOH, and subsequent introduction of a dimethylvinylsilyl tether at the 2'-hydroxyl gave the radical reaction substrate 1-[1-C-phenylseleno-2-O-dimethylvinylsilyl-3,5-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-ribopentofuranosyl]uracil (I). The photochem. radical atom-transfer reaction of I by using a high-pressure mercury lamp proceeded effectively in benzene to give the exo-cyclized PhSe-transferred product, in which (PhSe)2 proved to be essential as an additive for radical atom-transfer cyclization reactions. Subsequent phenylseleno-group elimination gave the sugar-protected 1'α-vinyluridine. With this procedure, 1-(1-C-ethenyl-β-D-ribopentofuranosyl)uracil and 1-(1-C-ethenyl-β-D-ribopentofuranosyl)cytosine, designed to be potential antitumor agents, were synthesized. This study is the first example of functionalization at the anomeric 1'-position of a **nucleoside** by starting from a natural **nucleoside** to produce a ribo-type 1'-modified **nucleoside.**

CC 33-9

ST Miscellaneous Descriptors
ethenylribopentofuranosyl uracil stereochem prepn; anomeric functionalized pyrimidine **ribonucleoside** stereochem prepn; phenylseleno **nucleoside** enolization stereoselective redn radical cyclization

RN 1719-58-0 (Chlorodimethylvinylsilane)
6553-96-4 (2,4,6-Triisopropylbenzenesulfonyl chloride)

RN 69304-38-7; 84828-97-7; 288103-31-1; 288103-32-2; 288103-33-3; 357610-01-6; 357610-08-3; 357610-10-7; 357610-11-8; 357610-13-0; 288103-29-7; 288103-30-0; 357610-02-7; **357610-03-8**; 357610-04-9; 357610-05-0; 357610-06-1; 357610-07-2; 357610-09-4; 357610-12-9; 357610-14-1

L89 ANSWER 33 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:173835 TOXCENTER

COPYRIGHT: Copyright 2005 ACS

DOCUMENT NUMBER: CA133172382340
TITLE: The degradation of the antitumor agent gemcitabine hydrochloride in an acidic aqueous solution at pH 3.2 and identification of degradation products
AUTHOR(S): Jansen, Patrick J.; Akers, Michael J.; Amos, Robert M.; Baertschi, Steven W.; Cooke, Gary G.; Dorman, Douglas E.; Kemp, Craig A. J.; Maple, Steven R.; Mccune, Karen A.
CORPORATE SOURCE: Lilly Research Laboratories, Pharmaceutical and Analytical Development Division, Eli Lilly and Company, Indianapolis, IN, 46285, USA.
SOURCE: Journal of Pharmaceutical Sciences, (2000) Vol. 89, No. 7, pp. 885-891.
CODEN: JPMSAE. ISSN: 0022-3549.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2000:522280
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20040210
ED Entered STN: 20011116
Last Updated on STN: 20040210
AB A study of the degradation kinetics of gemcitabine hydrochloride (2'-deoxy-2',2'-difluorocytidine) in aqueous solution at pH 3.2 was conducted. The degradation of gemcitabine followed pseudo first-order kinetics, and rate consts. were determined at four different temps. These rates were used to construct an Arrhenius plot from which degradation rates at lower temps. were extrapolated and activation energy calculated Four major degradation products were identified. Only one of these degradation products, the uridine analog of gemcitabine, was a known degradation product of gemcitabine and was identified by comparison with synthesized material. The other three degradation products were isolated and characterized by spectroscopic techniques. Two of these products were determined to be the diastereomeric 6-hydroxy-5,6-dihydro-2'-deoxy-2',2'-difluorouridines, and the other product was determined to be O6,5'-cyclo-5,6-dihydro-2'-deoxy-2',2'-difluorouridine. The mechanisms of formation of these degradation products are discussed.
CC 33-9
ST Miscellaneous Descriptors
nucleoside gemcitabine degrdn acidic kinetic activation energy
RN 122111-03-9 (Gemcitabine hydrochloride)
RN 114248-23-6; 294177-29-0; 294177-30-3; **294177-31-4**

L89 ANSWER 34 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:120285 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA13023308361X
TITLE: Effects of a high-affinity antibody fragment on DNA polymerase reactions near a (6-4) photoproduct site
AUTHOR(S): Kobayashi, Hiroyuki; Sato, Kousuke; Komatsu, Yasuo; Morioka, Hiroshi; Stewart, Jon D.; Tsurimoto, Toshiki; Ohtsuka, Eiko
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Hokkaido University, Sapporo, 060-0812, Japan.
SOURCE: Photochemistry and Photobiology, (1999) Vol. 69, No. 2, pp. 226-230.
CODEN: PHCBAP. ISSN: 0031-8655.
COUNTRY: JAPAN
DOCUMENT TYPE: Journal

FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1999:124202
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020509
ED Entered STN: 20011116
Last Updated on STN: 20020509
AB Pyrimidine (6-4) pyrimidone photodimers are major photoproducts that have mutagenic and carcinogenic consequences. One major reason for these biol. effects of (6-4) photoproducts may be base mispairing/DNA replication errors due to hydrogen bonding to bases opposite these damaged sites. We synthesized a modified 41-mer DNA containing a (6-4) photoproduct using a preformed building block, then employed it as a template for primer extension reactions catalyzed by Klenow fragment and DNA polymerases α, β and δ (pol α, pol β and pol δ).
None of these DNA polymerases were able to bypass the (6-4) photoproduct and elongation terminated at or near the 3'-pyrimidone of the photoproduct, depending on the dNTP concentration When a single-chain Fv (scFv)
with high affinity for the (6-4) photoproduct was included in the polymerization
reaction, DNA synthesis was inhibited at base positions four, six, eight or eight **nucleotides** prior to the 3'-pyrimidone by Klenow fragment, pol α, pol β or pol δ, resp. These results suggest that the scFv can bind to the template DNA containing a (6-4) photoproduct and inhibit extension reactions by polymerases.
CC 7-4
ST Miscellaneous Descriptors
pyrimidine pyrimidone photodimer DNA polymerase scFv primer extension
RN 9012-90-2 (DNA polymerase)
RN **100850-36-0**

L89 ANSWER 35 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:151479 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA12705061872Y
TITLE: Mutagenic properties of the T-C cyclobutane dimer
AUTHOR(S): Horsfall, Michael J.; Borden, Angela; Lawrence, Christopher W.
CORPORATE SOURCE: Dep. Biophys., Univ. Rochester Sch. Med. Dent., Rochester, NY, 14642, USA.
SOURCE: Journal of Bacteriology, (1997) Vol. 179, No. 9, pp. 2835-2839.
CODEN: JOBAAY. ISSN: 0021-9193.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1997:303515
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020605
ED Entered STN: 20011116
Last Updated on STN: 20020605
AB G·C→A·T transitions within T-C or C-C bipyrimidine sequences are by far the most frequent class of mutation induced by 254-nm UV irradiation in most genes and species investigated, but the reason for the high degree of mutability and specificity at these sites is uncertain. Some data implicate the deamination of cytosine to uracil as a possible cause, but other results appear to indicate that the rate of deamination is too low for this to be significant in Escherichia coli. If deamination

is not the cause, the high degree of mutability must presumably reflect the inherent properties of T-C and C-C dimers. The authors investigated this question by transfecting excision-deficient and excision-proficient strains of E. coli with single-stranded vectors that carried a site-specific cis-syn T-C cyclobutane dimer and by analyzing the **nucleotide** sequences of replicated vector products. The authors found that replication past the T-C dimer, like replication past its T-C and U-U counterparts, is in fact >95% accurate and that the frequencies of bypass are also very similar for these photoproducts. Since the T-C dimer appears to be only weakly mutagenic, the high frequency of UV-induced mutations at T-C sites presumably depends on some other process, such as deamination, although the mechanism remains to be established.

CC 4-6

ST Miscellaneous Descriptors
TC cyclobutane dimer mutagenicity

RN **97802-46-5** (Thymidine-(2'-deoxycytidine) cis,syn-cyclobutane dimer)
191347-50-9 (Thymine-Cytosine cis,syn-cyclobutane dimer)

L89 ANSWER 36 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:157148 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA12505058945C
TITLE: Definitive solution structures for the 6-formylated versions of 1-(β-D-ribofuranosyl)-, 1-(2'-deoxy-β-D-ribofuranosyl)-, and 1-β-D-arabinofuranosyluracil, and of thymidine
AUTHOR(S): Groziak, Michael P.; Lin, Ronghui; Stevens, William C.; Wotring, Linda L.; Townsend, Leroy B.; Balzarini, J.; Mitvrouw, M.; De Clercq, E.
CORPORATE SOURCE: Dep. Chem. Biochem., Southern Illinois Univ., Carbondale, IL, 62901-4409, USA.
SOURCE: Nucleosides & Nucleotides, (1996) Vol. 15, No. 5, pp. 1041-1057.
CODEN: NUNUD5. ISSN: 0732-8311.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1996:278111
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020730

ED Entered STN: 20011116
Last Updated on STN: 20020730

AB ROESY and NOESY NMR spectroscopic analyses of the ribofuranosyl (I), 2'-deoxyribofuranosyl (II), and arabinofuranosyl (III) derivs. of 6-formyluracil in (CD3)2SO and D2O solns. have established that each exclusive 7,05'-cyclic hemiacetal diastereomer of I and II and the major 7,02'-cyclic hemiacetal diastereomer of III possess the 7R configuration. In addition, (7R)-III has been shown to be thermodynamically more stable than (7S)-III, contrary to previous indications. A new, higher yielding synthetic route to I has been developed, II has been obtained for the first time in crystalline form, the route to III has been modified to better accommodate large scale prepns., and a new, fourth member of this class, 6-formylthymidine, has been synthesized and its solution structures in (CD3)2SO, D2O and CD3OD have been determined Antitumor and antiviral evaluations of I-III have revealed no significant levels of activity.

CC 33-9

ST Miscellaneous Descriptors
formyluracil **nucleoside** prepn soln structure; virucide

formyluracil **nucleoside**; neoplasm inhibitor formyluracil **nucleoside**; formylthymidine prepn
RN 14161-00-3; 138386-08-0; **149832-06-4**; 149884-54-8; 149884-55-9; 177779-24-7; 177779-25-8; 177779-31-6; 177779-32-7; 3083-77-0; 40733-26-4; 102147-76-2; 149832-01-9; 177779-23-6; 177779-26-9; 177779-27-0; 177779-28-1; 177779-29-2; 177779-30-5

L89 ANSWER 37 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:214373 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA123253329802
TITLE: Synthesis and biochemical evaluation of RNA containing an intrahelical disulfide crosslink
AUTHOR(S): Allerson, Charles R.; Verdine, Gregory L.
CORPORATE SOURCE: Dep. Chemistry, Harvard Univ., Cambridge, MA, 02138, USA.
SOURCE: Chemistry & Biology, (1995) Vol. 2, No. 10, pp. 667-75. CODEN: CBOLE2. ISSN: 1074-5521.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1995:918378
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020903
ED Entered STN: 20011116
Last Updated on STN: 20020903
AB Several factors impede the elucidation of RNA structure and function by x-ray and NMR methods, including the complexity of folded RNA motifs, the tendency of RNA to aggregate, and its ability to fold into multiple isomeric structures. The ability to constrain the process of RNA folding to give a single, homogenous product would assist these investigations. The authors therefore set out to develop a synthetic procedure for the site-specific insertion of a disulfide crosslink into **oligoribonucleotides.** The authors also examined the ability of a crosslinked species to serve as a substrate for ricin, an RNA glycosylase. A convertible **nucleoside** derivative (_C) suitable for the site-specific introduction of N4-alkyl-cytidine residues into RNA has been developed. The corresponding _C phosphoramidite was employed in the synthesis of an 8-mer **oligonucleotide**, 5'-_CGGAGA_CG-3', which was then efficiently converted to an 8-mer containing two S-protected N4-(2-thioethyl)C residues. Upon deprotection and air oxidation, the 8-mer efficiently formed an intramol. disulfide bond, yielding a GAGA tetraloop presented on a two-base pair _CpG disulfide crosslinked ministem. The authors show that this ministem-loop is an excellent substrate for ricin. Control 8-mers lacking the disulfide crosslink were substantially poorer substrates for ricin. The **nucleoside** chemical described here should be generally useful for the site-specific introduction of a range of non-native functional groups into RNA. The authors have used this chemical to constrain an RNA ministem through introduction of an intrahelical disulfide crosslink. That this tetraloop substrate linked to a two base-pair ministem is efficiently processed by ricin is clear evidence that ricin makes all of its energetically favorable contacts to the extreme end of the stem-loop structure, and that the two base pairs of the stem abutting the loop remain intact during recognition and processing by ricin.
CC 6-2
ST Miscellaneous Descriptors
RNA intrahelical disulfide crosslink
RN 170713-04-9; **170713-05-0**; 170713-06-1; 170713-07-2; 170782-01-1; 170713-09-4; 170713-08-3

L89 ANSWER 38 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:158995 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA12107073044U
TITLE: Novel Series of TSAO-T Derivatives. Synthesis and Anti-HIV-1 Activity of 4-, 5-, and 6-Substituted Pyrimidine Analogs
AUTHOR(S): San-Felix, Ana; Velazquez, Sonsoles; Perez-Perez, Maria Jesus; Balzarini, Jan; De Clercq, Erik; Camarasa, Maria Jose
CORPORATE SOURCE: Instituto de Quimica Medica (CSIC), Madrid, 28006, Spain.
SOURCE: Journal of Medicinal Chemistry, (1994) Vol. 37, No. 4, pp. 453-60.
CODEN: JMCMAR. ISSN: 0022-2623.
COUNTRY: SPAIN
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1994:473044
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020910
ED Entered STN: 20011116
Last Updated on STN: 20020910
AB Several 4-, 5-, and 6-substituted pyrimidine analogs of the new anti-HIV-1 lead compound [1-[2',5'-bis-O-(tert-butyldimethylsilyl)-β-D-ribofuranosylthymine]-3'-spiro-5''-(4''-amino-1'',2''-oxathiole 2'',2''-dioxide)] (TSAO-T) (I) were prepared and evaluated as inhibitors of HIV-1 and HIV-2 replication in cell cultures. Reaction of 1,2-di-O-acetyl-5-O-benzoyl-3-C-cyano-3-O-mesyl-D-ribofuranose with 5-substituted pyrimidine bases, followed by treatment with Cs2CO3, afforded, stereoselectively, β-D-ribofuranosyl-3'-**spironucleosides.** 2',5'-O-Deacylation and subsequent treatment with tert-butyldimethylsilyl chloride gave the TSAO-5-substituted pyrimidine derivs. Reaction of 5-halogen-TSAO derivs. with **nucleophiles** gave 6-substituted-TSAO analogs. Treatment of TSAO-pyrimidine analogs with POCl3/1,2,4-triazole and methylamine or dimethylamine afforded the 4-substituted pyrimidine compds. Several substituted TSAO-thymine, TSAO-uracil, and TSAO-cytosine derivs. were superior to their unsubstituted TSAO congeners with regard to their antiviral and/or cytotoxic properties.
CC 1-3
ST Miscellaneous Descriptors
HIV virus pyrimidine **nucleoside** analog prepn; virucide HIV pyrimidine **nucleoside** analog prepn; TSAOT deriv virucide HIV prepn structure
RN 51-20-7 (5-Bromouracil)
51-21-8 (5-Fluorouracil)
54-20-6 (5-(Trifluoromethyl)uracil)
696-07-1 (5-Iodouracil)
141781-17-1Q (derivs.)
RN 151215-43-9; 141845-83-2; 142102-75-8; 142102-77-0; 142102-78-1; 142385-63-5; 153364-37-5; 153364-38-6; 153364-39-7; **153364-40-0**; 153364-41-1; 153364-42-2; 153364-43-3; 153364-44-4; 153364-45-5; 153364-46-6; 153364-59-1; 153364-60-4; 153364-61-5; 153364-62-6; 153364-56-8; 153364-47-7; 153364-48-8; 153364-49-9; 153364-50-2; 153364-51-3; 153364-52-4; 153364-53-5; 153364-54-6; 153364-55-7; **153364-57-9**; 153364-58-0

L89 ANSWER 39 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:138765 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA12217208511N
TITLE: Insight into the chemical mechanism of thymidylate synthase-catalyzed reaction through the evaluation of chemical models: the role of C6 sulfhydryl addition during the reductive elimination step of the reaction
AUTHOR(S): Wang, Binghe; Kagel, John R.; Mertes, Mathias P.; Bowman-Janes, Kristin
CORPORATE SOURCE: Department Medicinal Chemistry, University Kansas, Lawrence, KS, 66045, USA.
SOURCE: Bioorganic Chemistry, (1994) Vol. 22, No. 4, pp. 405-20. CODEN: BOCMBM. ISSN: 0045-2068.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1995:328015
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020903
ED Entered STN: 20011116
Last Updated on STN: 20020903
AB Thymidylate synthase (I) catalyzes the last step of the de novo synthesis of dTMP, and has long been a target for the development of effective anticancer agents. Three model compds. were used to study the effect of C6 **nucleophilic** addition on the reductive elimination step of the I-catalyzed reaction. The results suggested that C6 addition facilitates the reductive elimination of the dihydrofolate moiety of the ternary intermediate. Therefore, the reaction pathway with the participation of C6 SH addition during the reductive elimination process is the energetically favored process. Consequently, the elimination of the Cys SH group from the C6 position is the last step of the reaction before the dissociation of the products from the enzyme.
CC 7-4
ST Miscellaneous Descriptors
thymidylate synthase mechanism model
RN 9031-61-2 (Thymidylate synthase)
RN 149204-06-8; 161986-78-3; 161986-79-4; 3816-77-1; 362-43-6; 2073-43-0; 37085-43-1; 60170-16-3; 161986-80-7; 161986-81-8; 161986-82-9; 161986-83-0; 161986-84-1; **65820-77-1**; 77421-71-7; 161986-85-2

L89 ANSWER 40 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:51516 TOXCENTER
DOCUMENT NUMBER: PubMed ID: 8332471
TITLE: Solution structure of nucleic acid photoadduct, deoxy-m5HO6-uridylyl(5-5)(3'-5')deoxyuridine by NMR and restrained molecular dynamics
AUTHOR(S): Kim J K; Soni S D; Wallace J C; Alderfer J L
CORPORATE SOURCE: Biophysics Department, Roswell Park Cancer Institute, Buffalo, NY 14263
CONTRACT NUMBER: CA16056 (NCI)
CA39027 (NCI)
RR02013 (NCRR)
+
SOURCE: Nucleic acids research, (1993 Jun 11) 21 (11) 2755-9. Journal Code: 0411011. ISSN: 0305-1048.
COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDLINE
OTHER SOURCE: MEDLINE 93324343

LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20011116
ED Entered STN: 20011116
Last Updated on STN: 20011116
AB Sensitized UV-B irradiation (sunlamps) of the **dinucleoside** monophosphate, d-TpF (F = fluorouracil), produces the usual cyclobutane-type photodimer and an additional defluorinated 5-5 photoadduct, d-T5p5U. In d-T5p5U, the original C5 = C6 structure is modified such that the C5 (d-T5p-) is covalently bonded with the C5 (-p5U) (where the fluorine had been) and the C6 (d-T5p-) acquires an OH group. 2D NOE data and the results of J-coupling analysis are used as constraints to refine structures of d-T5p5U in restrained molecular dynamics calculations. The structures obtained show the most probable **chiralities** of the C5 and C6 atoms of the Thy-portion to be 5R and 6R, respectively. The orientation of the CH3- and uracil-groups are pseudo-axial and pseudo-equatorial, respectively, with respect to the C5 atom. Glycosidic angles are high-anti and anti for the d-T5p- and the -p5U residue, respectively. C3'-endo like sugar puckering is predominant in the d-T5p- residue while C2'-endo like puckering is predominant at the -p5U residue.
CT *Dinucleoside Phosphates
Dinucleoside Phosphates: CS, chemical synthesis
*Dinucleoside Phosphates: RE, radiation effects
Magnetic Resonance Spectroscopy: MT, methods
Mathematics
Models, Molecular
Molecular Conformation
Molecular Structure
Pyrimidine Dimers
Research Support, U.S. Gov't, P.H.S.
Solutions
*Ultraviolet Rays
RN **149731-72-6** (deoxythymidine phosphate fluorouridine)
CN 0 (**Dinucleoside** Phosphates); 0 (Pyrimidine Dimers); 0 (Solutions)

L89 ANSWER 41 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:154945 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA11905049808J
TITLE: Novel types of N6,2'-**cyclonucleosides**
AUTHOR(S): Tronchet, Jean M.; Benhamza, Rachid; Bernardinelli, Gerald
CORPORATE SOURCE: Dep. Pharm. Chem., Fac. Sci., Geneva, 1211, Switz..
SOURCE: Nucleosides & Nucleotides, (1993) Vol. 12, No. 1, pp. 55-71.
CODEN: NUNUD5. ISSN: 0732-8311.
COUNTRY: SWITZERLAND
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1993:449808
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020917
ED Entered STN: 20011116
Last Updated on STN: 20020917
AB Upon oxidation followed by treatment with hydroxylamine, the 3',5'-diblocked uridine gave the expected oxime I together with the N6,2'-**cyclonucleoside** II formed by **nucleophilic** attack of hydroxylamine at both C-6 and C-2' positions. Reduction of I took place

predominantly from the α face and the major D-arabino compound obtained gave the **cyclonucleoside** III via Michael type addition The structures of the novel **cyclonucleosides**, particularly their configuration at C-6 were established by x-ray diffraction.
CC 33-9
ST Miscellaneous Descriptors
cyclonucleoside prepn configuration conformation virucide; bactericide **cyclonucleoside** prepn; **nucleoside** cyclo prepn configuration conformation; mol structure **cyclonucleoside** prepn conformation
RN 69304-38-7; 129076-85-3; 129076-93-3; 129076-94-4; 129076-82-0; 129076-83-1; **129076-87-5**; 129076-88-6; 129076-89-7; 148527-75-7; 129076-90-0; 129076-86-4

L89 ANSWER 42 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:160052 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA11909090122U
TITLE: Enzymic analysis of **oligonucleotides** containing cyclobutane pyrimidine photodimers with a cleaved intradimer phosphodiester linkage
AUTHOR(S): Liuzzi, Michel; Paterson, Malcolm C.
CORPORATE SOURCE: Dep. Med., Cross Cancer Inst., Edmonton, AB, T6G 1Z2, Can..
SOURCE: Journal of Biological Chemistry, (1992) Vol. 267, No. 31, pp. 22421-7.
CODEN: JBCHA3. ISSN: 0021-9258.
COUNTRY: CANADA
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1993:490122
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020917
ED Entered STN: 20011116
Last Updated on STN: 20020917
AB Recent studies indicate that enzymic hydrolysis of the intradimer phosphodiester linkage constitutes an early reaction in processing UV light-induced cis-syn-cyclobutane pyrimidine dimers in cultured human fibroblasts. Before characterizing the resultant modified dimer sites in cellular DNA, it is necessary to establish exptl. conditions that can distinguish backbone-nicked from intact dimers. A model substrate, i.e., p(dT)10<>p(dT)10 containing a dimer with a ruptured sugar-phosphate bond, was constructed and the products of its reaction with snake venom phosphodiesterase and alkaline phosphatase, an enzymic digestion mixture known to release dimers from UV-treated poly(dA)·poly(dT) within **trinucleotides** with the photoproduct intact at the 3'-end (d-TpT<p>T) determined The model substrate was prepared by (i) end labeling p(dT)9 using terminal **deoxynucleotidyl** transferase and [3H]thymine-labeled TTP, and (ii) annealing the chromatog. purified p(dT)10 oligomers to poly(dA) followed by UV (290 nm)-induced ligation. Photoligated 20-mers with one radioactive and modified internal dimer were isolated and enzymically digested. High performance liquid chromatog. anal. of the reaction products revealed a novel trithymidylate with its backbone severed at the 3'-terminus (d-TpT<>dT), demonstrating that this procedure could discriminate between intact and modified dimers. The procedure was then exploited to show that (i) Escherichia coli DNA photolyase can monomerize, albeit inefficiently, backbone-ruptured dimers and (ii) phage T4 **polynucleotide** kinase can catalyze the phosphorylation of d-TpT<>dT, thus facilitating the development of a sensitive postlabeling

assay suitable for modified dimer detection under biol. relevant conditions.
CC 8-1
ST Miscellaneous Descriptors
oligonucleotide cyclobutane pyrimidine photodimer enzymic analysis
RN 9025-82-5 (Phosphodiesterase)
37290-70-3 (DNA photolyase)
RN 54284-63-8; 54284-62-7; 143502-43-6; **113507-39-4**; 9001-78-9; 9027-67-2; 149149-07-5; 37211-65-7

L89 ANSWER 43 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:136639 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA11621207416Z
TITLE: Replication inhibition and translesion synthesis on templates containing site- specifically placed cis-diamminedichloroplatinum(II) DNA adducts
AUTHOR(S): Comess, Kenneth M.; Burstyn, Judith N.; Essigmann, John M.; Lippard, Stephen J.
CORPORATE SOURCE: Dep. Chem., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA.
SOURCE: Biochemistry, (1992) Vol. 31, No. 16, pp. 3975-90. CODEN: BICHAW. ISSN: 0006-2960.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1992:207416
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20021008
ED Entered STN: 20011116
Last Updated on STN: 20021008
AB A series of site-specifically platinated, covalently closed circular M13 genomes (7250 bp) was constructed in order to evaluate the consequences of DNA template damage induced by the anticancer drug cis-diamminedichloroplatinum(II) (cis-DDP). The synthesis and characterization of genomes containing the intrastrand crosslinked adducts cis-[Pt(NH3)2{d(ApG)-N7(1),-N7(2)}], cis-[Pt(NH3)2{d(GpCpG)-N7(1),-N7(3)}], and trans-[Pt(NH3)2{d(CpGpCpG)-N3(1),-N7(4)}] are reported. These constructs, as well as the previously reported M13 genome containing a site-specifically placed cis-[Pt(NH3)2{d(GpG)-N7(1),-N7(2)}] adduct, were used to study replication in vitro. DNA synthesis was initiated from a position approx. 177 **nucleotides** 3' to the individual adducts, and was terminated either by the adducts or by the end of the template, located approx. 25 **nucleotides** on the 5' side of the adducts. Anal. of the products of these reactions by gel electrophoresis revealed that, on average, bypass of most of the cis-DDP adducts occurred in approx. 10% of the cases and that the cis-[Pt(NH3)2{d(GpG)-N7(1),-N7(2)}] intrastrand cross-link is the most inhibitory lesion. The cis-[Pt(NH3)2{d(GpCpG)-N7(1),-N7(3)}] adduct allowed a higher frequency of such translesion synthesis (ca. 25%) for two of the polymerases studied, modified bacteriophage T7 polymerase and Escherichia coli DNA polymerase I (Klenow fragment). These enzymes have either low (Klenow) or no (T7) associated 3' to 5' exonuclease activity. Bacteriophage T4 DNA polymerase, which has a very active 3' to 5' exonuclease, was the most strongly inhibited by all three types of cis-DDP adducts, permitting only 2% translesion synthesis. This enzyme is therefore recommended for replication mapping studies to detect the location of cis-DDP-DNA adducts in a heterologous population. The major replicative enzyme of E. coli,

the DNA polymerase III holoenzyme, allowed <10% adduct bypass. Postreplication restriction enzyme cleavage studies established that the templates upon which translesion synthesis was observed contained platinum adducts, ruling out the possibility that the observed products were due to a small amount of contamination with unplatinated DNA. The effects on in vitro replication of a recently characterized adduct of trans-DDP were also evaluated. This adduct provided a poor block both to DNA polymerases and to restriction enzymes. The properties of this adduct in the M13 genome were investigated by postreplication sequence anal. of the translesion synthesis product. Polymerases can traverse through all of the major bifunctional cisplatin adducts formed in vitro and in vivo and strengthen the hypothesis that adduct-induced mutagenesis may occur through replication bypass.

CC 1-6

ST Miscellaneous Descriptors
cisplatin DNA adduct prepn characterization; platinum antitumor **oligonucleotide** adduct prepn

RN 15663-27-1 (Cisplatin)

RN 87411-79-8; 140663-33-8; **140676-17-1**; 20115-64-4; 140663-30-5; 140663-31-6; **140663-32-7**; 140850-14-2; 125137-94-2; 140696-58-8

L89 ANSWER 44 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:114923 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA11603015430C
TITLE: Metallocene antitumor agents. Solution and solid-state molybdenocene coordination chemistry of DNA constituents
AUTHOR(S): Kuo, Louis Y.; Kanatzidis, Mercouri G.; Sabat, Michal; Tipton, Andrew L.; Marks, Tobin J.
CORPORATE SOURCE: Dep. Chem., Northwestern Univ., Evanston, IL, 60208, USA.
SOURCE: Journal of the American Chemical Society, (1991) Vol. 113, No. 24, pp. 9027-45.
CODEN: JACSAT. ISSN: 0002-7863.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1992:15430
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20021001

ED Entered STN: 20011116
Last Updated on STN: 20021001

AB A chemical-physicochem. investigation of the coordination chemical of aqueous molybdenocene dichloride with DNA constituents is reported. The goals were to investigate the aqueous solution chemical of Cp2MoCl2 (Cp = η5-C5H5) and to establish the nature of Mo(IV) coordination to DNA building blocks including representative 2'-**deoxynucleotide**-5'-monophosphates and alkylated **nucleobases** under physiol. conditions (mM concentration in Cp2MoCl2 and pH = 7.2-7.4). This coordination chemical can be readily elucidated using FT NMR techniques. It was observed that the Mo-Cp ligation is hydrolytically stable while chloride hydrolysis is complete and extremely rapid and that the coordination of aqueous Cp2MoCl2 to DNA constituents is radically different from that of Cp2VCl2. On the NMR time scale and in the absence of other competing ligands, Cp2MoCl2(aq) coordinates to both the **nucleobase** (N) and phosphate (O) moieties of **mononucleotides** in a relatively nonlabile manner that effects major conformational changes within the **mononucleotide.** In addition, the crystal structures of the model compds., [Cp2Mo(9-methyladenyl)][PF36], [Cp2Mo(1-methylcytosyl)][PF6], and

[Cp2Mo(2'-deoxyguanosine-5'-monophosphate)]2, which confirm the spectroscopically derived solution coordination patterns and provide important metrical details are presented. These results and their implications for Cp2Mo2+ binding to DNA vis-a-vis that of cisplatin are also discussed.

CC 1-6

ST Miscellaneous Descriptors
DNA molybdenocene coordination chem antitumor

RN 137719-64-3Q (complexes with molybdenocene)
12184-22-4Q (complexes with **nucleosides** and **nucleotide** bases)
700-00-5 (9-Methyladenine)
1122-47-0 (1-Methylcytosine)

RN 110825-78-0; 110825-80-4; 137719-68-7; 137742-04-2; **137742-05-3**; **137719-69-8**; 110825-82-6; 137719-66-5; 653-63-4; 33430-61-4

L89 ANSWER 45 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:149213 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA113131115746S
TITLE: Novel types of **cyclonucleosides**
AUTHOR(S): Tronchet, Jean M. J.; Benhamza, Rachid; Bernardinelli, Gerald; Geoffroy, Michel
CORPORATE SOURCE: Fac. Sci., Univ. Geneva, Geneva, CH-1211, Switz..
SOURCE: Tetrahedron Letters, (1990) Vol. 31, No. 4, pp. 531-4.
CODEN: TELEAY. ISSN: 0040-4039.
COUNTRY: SWITZERLAND
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1990:515746
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20021015

ED Entered STN: 20011116
Last Updated on STN: 20021015

AB Reduction of 2'-deoxy-2'-(hydroxyimino)uridine derivs. led to hydroxylamines (mostly arabino configuration) which on treatment with aromatic aldehydes afforded the corresponding nitrones which were reduced to hydroxylamines. The modified **nucleosides** bearing a hydroxyamino group at the 2'-position when of arabino configuration underwent conjugate addition onto the uracil ring leading to novel types of **cyclonucleosides** e.g., I (R = Ac, H, R1 = H, OMe) and II (R = aryl). The **cyclonucleosides** showed some antibacterial activity. The crystal structures of I (R = Ac, R1 = Me; R = R1 = H) were determined by x-ray diffraction methods.

CC 33-9

ST Miscellaneous Descriptors
nucleoside cyclo prepn bactericide; bactericide
cyclonucleoside prepn; hydroxylamine **cyclonucleoside** prepn HIV; **oxaazacyclonucleoside**; uridine hydroxyiminodeoxy redn; crystal structure **cyclonucleoside**; mol structure **cyclonucleoside**

RN 89-98-5 (2-Chlorobenzaldehyde)
98-03-3 (2-Thiophenecarboxaldehyde)
120-14-9 (3,4-Dimethoxybenzaldehyde)
148-53-8 (2-Hydroxy-3-methoxybenzaldehyde)

RN 2426-87-1; 84828-97-7; **129076-87-5**; 129076-85-3; 129076-90-0; 129077-05-0; 129077-06-1; 129077-07-2; 129077-08-3; 129077-09-4; 129077-10-7; 129077-11-8; 129110-00-5; 129076-86-4; 129076-82-0; 129076-83-1; 129077-01-6; 129077-02-7; 129077-03-8; 129077-04-9;

129076-88-6; 129076-89-7; 129076-99-9; 129077-00-5; 129076-95-5; 129076-97-7; **129076-84-2**; 129076-93-3; 129076-94-4; 129076-96-6; 129076-98-8; 129077-12-9; 129077-13-0; 129077-14-1; 129077-15-2; 129076-91-1; 129076-92-2

L89 ANSWER 46 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:137288 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA11101003311Y
TITLE: Enzymic analysis of isomeric trithymidylates containing ultraviolet light-induced cyclobutane pyrimidine dimers. II. Phosphorylation by phage T4 **polynucleotide** kinase
AUTHOR(S): Weinfeld, Michael; Liuzzi, Michel; Paterson, Malcolm C.
CORPORATE SOURCE: Dep. Med., Cross Cancer Inst., Edmonton, AB, T6G 1Z2, Can..
SOURCE: Journal of Biological Chemistry, (1989) Vol. 264, No. 11, pp. 6364-70.
CODEN: JBCHA3. ISSN: 0021-9258.
COUNTRY: CANADA
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1989:403311
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20021022
ED Entered STN: 20011116
Last Updated on STN: 20021022
AB Phage T4 **polynucleotide** kinase (EC 2.7.1.78) proved incapable of catalyzing the phosphorylation of thymidylyl-(3'→5')-thymidine containing either a cis-syn-cyclobutane pyrimidine dimer (d-T<p>T) or a 6-4'-[pyrimidin-2'-one]pyrimidine photoproduct (d-T[p]-T), and similarly the UV-modified compds. of (dT)3 bearing either photoproduct at their 5'-end (d-T<p>TpT and d-T[p]TpT). In contrast, the 3'-structural isomers of these **trinucleotides** (d-TpT<p>T and d-TpT[p]T) were phosphorylated at the same rate as the parent compound These phosphorylatable lesion-containing **oligonucleotides** are quant. released from UV-irradiated poly(dA)·poly(dT) by enzymic hydrolysis with snake venom phosphodiesterase and alkaline phosphatase (Liuzzi, M., et al., 1989). By combining this digestion regimen with phosphorylation by **polynucleotide** kinase and [γ-32P]ATP, pyrimidine dimers were quantitated at the fmol level following exposure of poly(dA)·poly(dT) and herring sperm DNA to biol. relevant UV fluences. The rate of dimer induction in the synthetic polymer, .apprx.10 dimers/106 **nucleotides**/Jm-2, was in close agreement with that obtained by conventional methods. Dimers were induced at 25% of this rate in the natural DNA. Further treatment of the phosphorylated **oligonucleotides** derived from irradiated herring sperm DNA with nuclease P1 released the labeled 5'-**nucleotide**, thus permitting anal. of the nearest-neighbor bases 5' to the lesions. A ratio was observed for pyrimidine-to-purine bases of almost 6:1, implicating tripyrimidine stretches as hotspots for UV-induced DNA damage.
CC 8-1
ST Miscellaneous Descriptors
UV trithymidylate cyclobutane pyrimidine dimer analysis
RN 1969-54-6 (Thymidylyl-(3'→5')-thymidine)
24939-09-1 (Poly(dA):poly(dT))
9025-82-5 (Phosphodiesterase)
54576-84-0 (Nuclease P1)
RN 2640-26-8; 37211-65-7; **4472-37-1**; **120995-96-2**;

113490-63-4; **113507-39-4**; **120977-20-0**;
120977-21-1; 9001-78-9

L89 ANSWER 47 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:137287 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA11101003310X
TITLE: Enzymic analysis of isomeric trithymidylates containing ultraviolet light-induced cyclobutane pyrimidine dimers. I. Nuclease P1-mediated hydrolysis of the intradimer phosphodiester linkage
AUTHOR(S): Liuzzi, Michel; Weinfeld, Michael; Paterson, Malcolm C.
CORPORATE SOURCE: Dep. Med., Cross Cancer Inst., Edmonton, AB, T6G 1Z2, Can..
SOURCE: Journal of Biological Chemistry, (1989) Vol. 264, No. 11, pp. 6355-63.
CODEN: JBCHA3. ISSN: 0021-9258.
COUNTRY: CANADA
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1989:403310
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20021022
ED Entered STN: 20011116
Last Updated on STN: 20021022
AB Recent findings suggest that enzymic hydrolysis of the intradimer phosphodiester bond may constitute the initial step in the repair of UV light-induced cyclobutane pyrimidine dimers in human cells. To examine the susceptibility of this phosphodiester linkage to enzyme-mediated hydrolysis, the **trinucleotide** d-TpTpT was UV-irradiated and the 2 isomeric compds. containing a cis-syn-cyclobutane dimer were isolated by HPLC and treated with various DNases. Snake venom phosphodiesterase hydrolyzed only the 3'-phosphodiester group in the 5'-isomer (d-T<p>TpT) but was totally inactive toward the 3'-isomer (d-TpT<p>T). In contrast, calf spleen phosphodiesterase only operated on the 3'-isomer by cleaving the 5'-**internucleotide** bond. Kinetic anal. revealed that (i) the activity of snake venom phosphodiesterase was unaffected by a dimer 5' to a phosphodiester linkage, (ii) the action of calf spleen phosphodiesterase was partially inhibited by a dimer 3' to a phosphodiester bond, and (iii) Escherichia coli phr B-encoded DNA photolyase reacted twice as fast with d-T<p>TpT as with d-TpT<p>T. Mung bean nuclease, nuclease S1, and nuclease P1 all cleaved the 5'-**internucleotide** linkage, but not the intradimer phosphodiester bond, in d-TpT<p>T. Both phosphate groups in d-T<p>TpT were refractory to mung bean nuclease or nuclease S1. Incubation to d-T<p>TpT with nuclease P1, however generated the novel compound d-T<>d-pTpT containing a severed intradimer phosphodiester linkage. Accordingly, nuclease P1 represents the 1st purified enzyme known to hydrolyze an intradimer phosphodiester linkage.
CC 8-1
ST Miscellaneous Descriptors
UV trithymidylate cyclobutane pyrimidine dimer analysis
RN 24939-09-1 (Poly(dA):poly(dT))
9025-82-5 (Phosphodiesterase)
9026-81-7 (Nuclease)
37288-25-8 (Nuclease S1)
37290-70-3 (DNA photolyase)
54576-84-0 (Nuclease P1)
RN 2640-26-8; **113490-63-4**; **113507-39-4**; 121150-95-6

L89 ANSWER 48 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:159923 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA11123211175J
TITLE: The in vitro and in vivo behavior of fluorine-18-labeled 5-fluoro-5,6-dihydrouracil **nucleosides**
AUTHOR(S): Visser, Gerard W. M.; Bijma, Anita T.; Dijksman, Jessica A. R.; Gorree, Geertrui C. M.; Van Walsum, Marijke; Herscheid, Jacobus D. M.
CORPORATE SOURCE: Radio-Nuclide-Cent., Free Univ., Amsterdam, 1007 MC, Neth..
SOURCE: Nuclear Medicine and Biology, (1989) Vol. 16, No. 4, pp. 351-7.
CODEN: NMBIEO. ISSN: 0883-2897.
COUNTRY: NETHERLANDS
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1989:611175
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20021022
ED Entered STN: 20011116
Last Updated on STN: 20021022
AB The isolation of the cis-5-[18F]fluoro-6-acetoxy diastereomers, products from the reaction of [18F]acetyl hypofluorite with 2'-deoxyuridine, uridine, and arabinofuranosyluracil in AcOH, acid, and the corresponding [18F]5-fluoro-5,06-anhydro-6-hydroxy-cyclouracil derivs. is described. As an evaluation of their possible use as prodrugs for the toxic 5-fluorouracil (5-FU), the in vitro behavior of these 2 new classes of 18F-labeled pyrimidines in water was determined In addition, the in vivo behavior of some of these compds. was studied in nude mice bearing either 5-FU-sensitive or 5-FU-resistant tumors.
CC 8-10
ST Miscellaneous Descriptors
fluorine 18 fluorodihydrouracil **nucleoside** metab tumor
RN 58-96-8 (Uridine)
696-06-0Q (**nucleosides**)
RN 951-78-0; 3083-77-0; 823-63-2; 72156-83-3; 67829-10-1; **119003-29-1**; **119003-31-5**; **119068-01-8**; **119068-05-2**; **119068-09-6**; **119068-10-9**; 119003-28-0; 119003-30-4; 119068-00-7; 119068-02-9; 119068-06-3; 119070-19-8; 106678-95-9; 119068-03-0; 119068-04-1; 119068-07-4; 119068-08-5; 119180-46-0; 119180-47-1

L89 ANSWER 49 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1987:126871 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA10625207299G
TITLE: FT-IR spectroscopic evidence of sugar ring conformational changes in GpC and CpG on platination and intercalation
AUTHOR(S): Okamoto, Koji; Benham, Victor; Theophanides, Theophile
CORPORATE SOURCE: Dep. Chem., Univ. Montreal, Montreal, QC, H3C 3J7, Can..
SOURCE: Inorganica Chimica Acta, (1987) Vol. 135, No. 3, pp. 207-10.
CODEN: ICHAA3. ISSN: 0020-1693.
COUNTRY: CANADA
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS

OTHER SOURCE: CAPLUS 1987:207299
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20021105
ED Entered STN: 20011116
Last Updated on STN: 20021105
AB An FT-IR spectroscopic study concerning changes in the conformation of sugar in the **dinucleotides** GpC [4785-04-0] and CpG [2382-65-2] on platination and intercalation is presented. The results are compared with the FT-IR spectral data of 5'-CMP [63-37-6], GMP [85-32-5], 3'-GMP [117-68-0] and their metal adducts. The spectra of free GpC, free CpG, proflavine-GpC [107022-01-5], proflavine-CpG [79328-21-5], and cis-[Pt(NH3)2(GpC)2] [92269-81-3] exhibit the diagnostic band at 800/cm which was assigned to a sugar phosphate vibrational mode and diagnostic of C3'-endo sugar pucker. In the case of 9-aminoacridine-GpC [108402-39-7] and cis-[Pt(NH3)2(CpG]+ [**92344-06-4**] the diagnostic bands of the C2'-endo and C3'-endo conformations are observed at 810-820 and near 800/cm, resp. The results are in good agreement with x-ray data. The IR diagnostic bands are important for distinguishing the sugar pucker conformational changes. As a conclusion, it seems that the binding of the anticancer drugs (intercalating or chemical bound) with d(GpG), d(GpC), or d(CpG) sequences in DNA may destroy the backbone sugar conformation of DNA by changing the sugar pucker to accommodate the strain caused by the presence of the drug.
CC 1-6
ST Miscellaneous Descriptors
antitumor DNA **nucleotides** sugar conformation; cisplatin **nucleotide** adduct sugar conformation
RN 63-37-6 (5'-CMP)
85-32-5 (GMP)
117-68-0 (3'-GMP)
RN 2382-65-2; 4785-04-0; 79328-21-5; 92269-81-3; **92344-06-4**; 107022-01-5; 108402-39-7

L89 ANSWER 50 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:38772 TOXCENTER
DOCUMENT NUMBER: PubMed ID: 4016218
TITLE: Crystal structure of the cis-syn photodimer of thymidylyl (3'-5') thymidine cyanoethyl ester
AUTHOR(S): Cadet J; Voituriez L; Hruska F E; Grand A
SOURCE: Biopolymers, (1985 May) 24 (5) 897-903.
Journal Code: 0372525. ISSN: 0006-3525.
COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDLINE
OTHER SOURCE: MEDLINE 85253040
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20011116
ED Entered STN: 20011116
Last Updated on STN: 20011116
CT Crystallography
DNA: RE, radiation effects
*Dinucleoside Phosphates
*Molecular Conformation
Photochemistry
Research Support, Non-U.S. Gov't
*Thymine **Nucleotides**: AN, analysis
Ultraviolet Rays
RN 9007-49-2 (DNA)

97423-58-0 (thymidylyl(3'-5')thymidine cyanoethyl ester)
CN 0 (**Dinucleoside** Phosphates); 0 (Thymine **Nucleotides**)

L89 ANSWER 51 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:126967 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA10423203193D
TITLE: Conformations of **deoxydodecanucleotides** with pyrimidine (6-4)-pyrimidone photoadducts
AUTHOR(S): Rao, Shashidhar N.; Kollman, Peter A.
CORPORATE SOURCE: Dep. Pharm. Chem., Univ. California, San Francisco, CA, 94143, USA.
SOURCE: Photochemistry and Photobiology, (1985) Vol. 42, No. 5, pp. 465-75.
CODEN: PHCBAP. ISSN: 0031-8655.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1986:203193
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20021112
ED Entered STN: 20011116
Last Updated on STN: 20021112
AB Mol. mech. simulations have been carried out of **dodecanucleotide** d(CGCGAAXYCGCG).d(CGCGX'Y'TTCGCG) with XY being CC, TC, TT, and CT and X'Y' being their corresponding base paired **dinucleotides** on the complementary strand. Simulations were also carried out with the corresponding pyrimidine (6-4)-pyrimidone photoadducts incorporated in these **dodecanucleotides.** As in the case of the cyclobutane dimer incorporated **dodecanucleotide** structures (Rao, S. N. et al., 1984), those regions of the DNA modified by 6-4 pyrimidine adducts are found to undergo little conformational changes except in the dimer region. The conformational characteristics of the 6-4 pyrimidine adduct incorporated structures seem to be influenced by the nature of the base at the 3' end of the dimer. Specifically, favorable H bonding interactions between the 5' end base and its preceding phosphate group are present in structures which have cytosine at the 3' end of the photodimer. The energetics of these structures relative to those without incorporated dimers have been discussed and the results have been analyzed in the light of the currently prevalent ideas on the role of the 6-4 photoadducts in mutagenesis in various organisms.
CC 8-10
ST Miscellaneous Descriptors
pyrimidine pyrimidone photoadduct **deoxydodecanucleotide** conformation
RN **102059-50-7**; **102059-53-0**; **102088-27-7**; 102136-28-7

L89 ANSWER 52 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:135324 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA10123203970T
TITLE: Cytidylyl (3'-5')guanosine **dinucleotides** give two platinum chelates with cis-diamminedichloroplatinum that are cytidine syn-anti conformational isomers
AUTHOR(S): Girault, Jean Pierre; Chottard, Genevieve; Lallemand, Jean Yves; Huguenin, Frederic; Chottard, Jean Claude
CORPORATE SOURCE: Lab. Chim., Ec. Norm. Super., Paris, 75231, Fr..
SOURCE: Journal of the American Chemical Society, (1984) Vol. 106,

No. 23, pp. 7227-32.
CODEN: JACSAT. ISSN: 0002-7863.
COUNTRY: FRANCE
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1984:603970
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20021119
ED Entered STN: 20011116
Last Updated on STN: 20021119
AB CpG ammonium salt [27553-01-1] and d(pCpG) ammonium salt [92269-83-5] react with cis[PtCl2(NH3)2] (cis-DDP) [15663-27-1] or cis-[Pt(NH3)2(H2O)2](NO3)2 [52241-26-6] to yield the resp. (CN3-GN7)-(cis-Pt(NH3)22+) adducts. Reaction of CpG with [PtBr(dien)]Br [15633-95-1] and monitoring the reaction with cis-DDP and its diaqua derivative indicates that the formation of the adduct is a 2-step process starting with N7-platination of the guanine residue. The ribo- and deoxy-(C-G)·cis-Pt chelates exist as C(anti)-G(anti) and C(syn)-G(anti) isomers; CD spectra of these diastereoisomers present a remarkable sign-inversion which can be related to their pseudohelical arrangement. These and other observations demonstrated that an equilibration process exists between the 2 isomeric Pt-chelates attributable to the rotation of the cytosine residue about its glycosidic N3-Pt bonds.
CC 1-6
ST Miscellaneous Descriptors
cytidylylguanidylate platinum chelation; diamminedichloroplatinum chelation cytidylylguanidylate
RN 7440-06-4Q (cytidylylguanidylate chelates)
RN 15633-95-1; 15663-27-1; 52241-26-6; 27553-01-1; 92269-83-5; **92269-77-7**; **92269-78-8**; 92269-79-9; 92269-80-2; 92269-81-3; 92269-82-4; **92344-06-4**; **92344-07-5**

L89 ANSWER 53 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1983:107949 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA09821172676Q
TITLE: Platinum-**oligonucleotide** structures and their relevance to platinum-DNA interaction
AUTHOR(S): Chottard, Jean Claude; Girault, Jean Pierre; Guittet, Eric R.; Lallemand, Jean Yves; Chottard, Genevieve
CORPORATE SOURCE: Lab. Chim., Ec. Norm. Super., Paris, 75231/05, Fr..
SOURCE: ACS Symposium Series, (1983) Vol. 209, No. Platinum, Gold, Other Met. Chemother. Agents: Chem. Biochem., pp. 125-45.
CODEN: ACSMC8. ISSN: 0097-6156.
COUNTRY: FRANCE
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1983:172676
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20021126
ED Entered STN: 20011116
Last Updated on STN: 20021126
AB The stoichiometric reactions of 9 oxy and deoxyguanine and/or cytosine containing **dinucleotides** with cis-[Pt(NH3)2(H2O)2](NO3)2 [52241-26-6] (10-5-5 + 10-4 M) in water gave monomeric Pt **dinucleotide** chelates in every case. The complexes were isolated by high-pressure liquid chromatog. and characterized by NMR and CD analyses.

GpG [3353-33-1], d(GpG) [15180-30-0], And d(pGpG) [26467-04-9] gave a single N7-N7 anti-anti complex [81125-55-5]. CpC [2536-99-4] And d(pCpC) [26467-02-7] gave a single N3-N3 syn-anti complex. CpG [2382-65-2] And d(pCpG) [15623-43-5] gave a mixture of N3-N7 C anti-G anti and C syn-G anti isomers in equilibrium GpC [4785-04-0] And d(pGpC) [2402-35-9] gave 2 couples of N7-N3 isomers: G syn-C anti, G syn-C syn (in equilibrium) and G anti-C anti, G anti-C syn. The results obtained point to a particular chelating aptitude of the anti-anti GG sequence. Accordingly, the stoichiometric reaction of the **hexanucleotide** d(TpGpGpCpCpA) [84640-20-0] with the Pt complex gives quant. the GN7-GN7 chelate. These results are in favor of the hypothesis of Pt intrastrand cross-linking of adjacent guanines in DNA.

CC 1-6
ST Miscellaneous Descriptors
platinum complex DNA interaction; **nucleotide** platinum complex
RN 7440-06-4Q (complexes)
RN 81119-95-1; 81119-96-2; 81125-55-5; **85528-65-0**; **85538-80-3**; 52241-26-6; 2382-65-2; 2402-35-9; 2536-99-4; 3353-33-1; 4785-04-0; 15180-30-0; 15623-43-5; 26467-02-7; 26467-04-9; 84640-20-0

L89 ANSWER 54 OF 84 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1978:85445 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA08825184831T
TITLE: Interaction of the anti-tumor drug cis-dichloroethylenediamineplatinum (cis-Pt(en)Cl2) with cytidylyl-3' → 5'-guanosine
AUTHOR(S): Jordanov, J.; Williams, R. J. P.
CORPORATE SOURCE: Lab. Chim. Coord., Univ. Louis Pasteur, Strasbourg, Fr..
SOURCE: Bioinorganic Chemistry, (1978) Vol. 8, No. 1, pp. 77-82. CODEN: BICHBX. ISSN: 0006-3061.
COUNTRY: FRANCE
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1978:184831
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20021210
ED Entered STN: 20011116
Last Updated on STN: 20021210
AB Chemical shifts in 1H NMR and Sephadex G-25 chromatog. were used to follow the reaction of Pt(en)Cl2 with the **dinucleotide**, C3'p5'G (cytidylyl-3'-phosphate 5'-guanosine), in aqueous solution and to sep. its products. Binding of the Pt occurred 1st at the cytosine, then at the guanine base. Two major complexes were formed, Pt-CpG and (Pt-CpG)2, which accounted for, resp., an internal and an external crosslinking effect.
CC 6-3
ST Miscellaneous Descriptors
platinum compd interaction cytidylylguanosine; antitumor drug interaction cytidylylguanosine
RN 50790-42-6; 66541-56-8; **66541-57-9**; 14096-51-6; 65-46-3; 118-00-3; 2382-65-2

=> d ibib ed ab hitstr 55-64
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, TOXCENTER, USPATFULL, WPIX, BIOSIS, CANCERLIT, BIOTECHNO, BIOTECHDS, SCISEARCH' - CONTINUE? (Y)/N:y

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L89 ANSWER 55 OF 84 USPATFULL on STN

ACCESSION NUMBER:	2004:307857 USPATFULL		
TITLE:	Antiviral nucleosides		
INVENTOR(S):	Kumar, Rakesh, Edmonton, CA, UNITED STATES		
	Agrawal, Babita, Edmonton, CA, UNITED STATES		
	Tyrrell, D. Orne J., Edmonton, CA, UNITED STATES		

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004242533	A1	20041202	
APPLICATION INFO.:	US 2004-477763	A1	20040629	(10)
	WO 2002-CA718		20020517	

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-291960P	20010518 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	BOZICEVIC, FIELD & FRANCIS LLP, 1900 UNIVERSITY AVE, SUITE 200, EAST PALO ALTO, CA, 94303
NUMBER OF CLAIMS:	83
EXEMPLARY CLAIM:	1
LINE COUNT:	4682

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

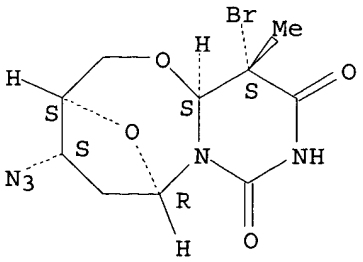
AB Disclosed are nucleosides which are useful in dignosing and treating viral infections, for example, infections caused by hepatitis B virus (HBV), and herpes viruses including Epstein Barr virus.

IT **224797-38-0P 475503-15-2P 475503-16-3P**
(preparation of acyclic nucleosides as antiviral and antitumor agents)

RN 224797-38-0 USPATFULL

CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 4-azido-11-bromohexahydro-11-methyl-, (3S,4S,6R,11S,11aS)- (9CI) (CA INDEX NAME)

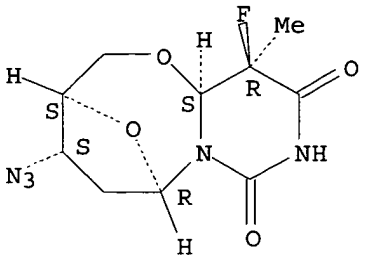
Absolute stereochemistry. Rotation (-).



RN 475503-15-2 USPATFULL

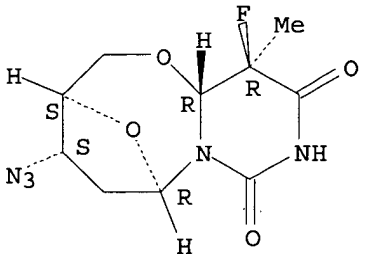
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 4-azido-11-fluorohexahydro-11-methyl-, (3S,4S,6R,11R,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



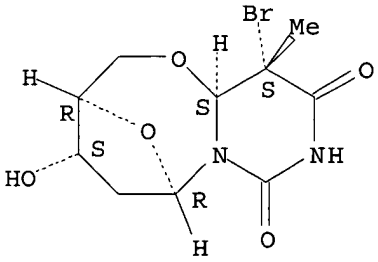
RN 475503-16-3 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 4-azido-11-fluorohexahydro-11-methyl-, (3S,4S,6R,11R,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



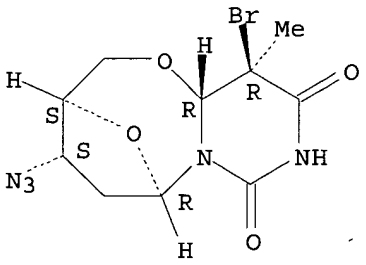
IT **41308-60-5P 224797-40-4P 475503-07-2P**
475503-08-3P 475503-09-4P 475503-10-7P
475503-11-8P 475503-12-9P 475503-13-0P
475503-14-1P 475503-17-4P 475503-18-5P
475503-19-6P 475503-20-9P 475503-21-0P
475503-22-1P 475503-23-2P 475503-24-3P
475503-25-4P 475503-26-5P 475503-27-6P
475503-28-7P 475503-29-8P 475503-30-1P
475503-31-2P 475991-46-9P
(preparation of acyclic nucleosides as antiviral and antitumor agents)
RN 41308-60-5 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 11-bromohexahydro-4-hydroxy-11-methyl-, [3R-(3α,4α,6α,11α,11aα)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



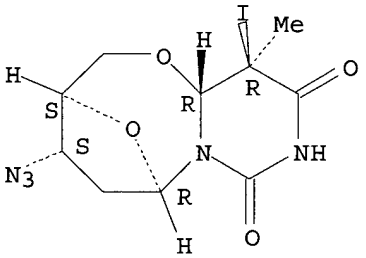
RN 224797-40-4 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 4-azido-11-bromohexahydro-11-methyl-, (3S,4S,6R,11R,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



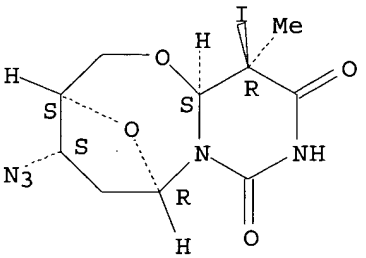
RN 475503-07-2 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 4-azidohexahydro-11-iodo-11-methyl-, (3S,4S,6R,11R,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



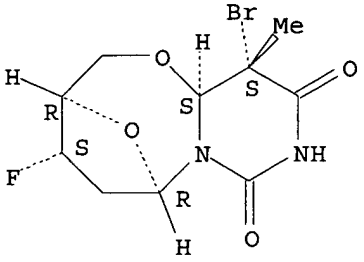
RN 475503-08-3 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 4-azidohexahydro-11-iodo-11-methyl-, (3S,4S,6R,11R,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



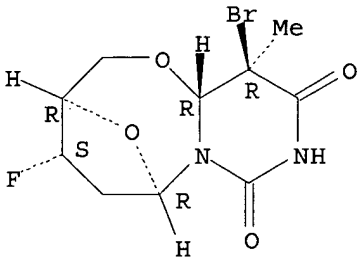
RN 475503-09-4 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 11-bromo-4-fluorohexahydro-11-methyl-, (3R,4S,6R,11S,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



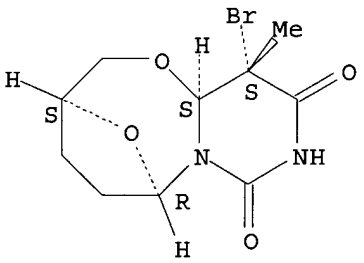
RN 475503-10-7 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 11-bromo-4-fluorohexahydro-11-methyl-, (3R,4S,6R,11R,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



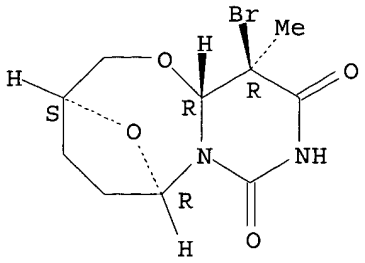
RN 475503-11-8 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 11-bromohexahydro-11-methyl-, (3S,6R,11S,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



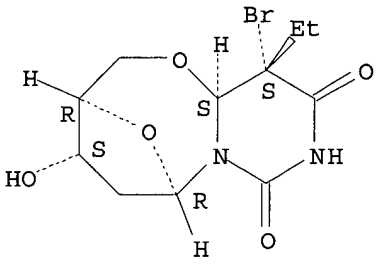
RN 475503-12-9 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 11-bromohexahydro-11-methyl-, (3S,6R,11R,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



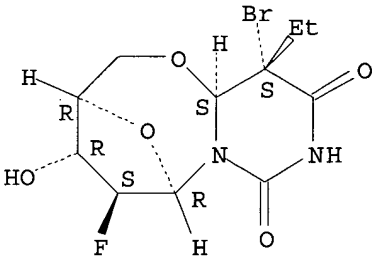
RN 475503-13-0 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 11-bromo-11-ethylhexahydro-4-hydroxy-, (3R,4S,6R,11S,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



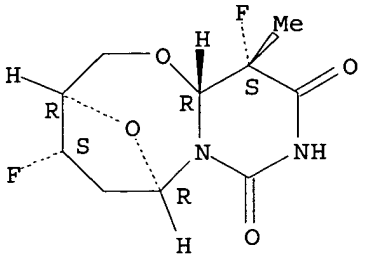
RN 475503-14-1 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 11-bromo-11-ethyl-5-fluorohexahydro-4-hydroxy-, (3R,4R,5S,6R,11S,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



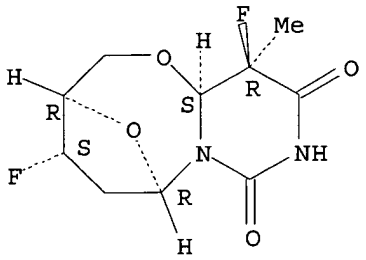
RN 475503-17-4 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 4,11-difluorohexahydro-11-methyl-, (3R,4S,6R,11S,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



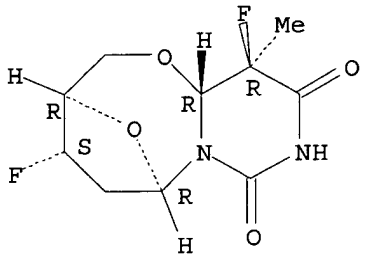
RN 475503-18-5 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 4,11-difluorohexahydro-11-methyl-, (3R,4S,6R,11R,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



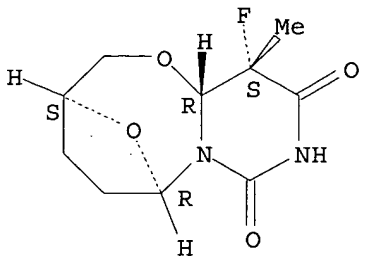
RN 475503-19-6 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 4,11-difluorohexahydro-11-methyl-, (3R,4S,6R,11R,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



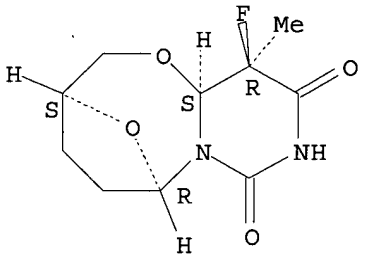
RN 475503-20-9 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 11-fluorohexahydro-11-methyl-, (3S,6R,11S,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



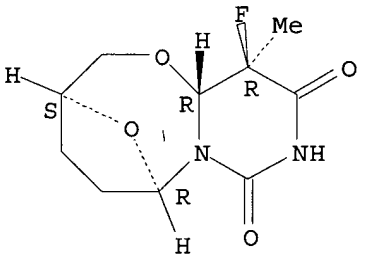
RN 475503-21-0 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 11-fluorohexahydro-11-methyl-, (3S,6R,11R,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



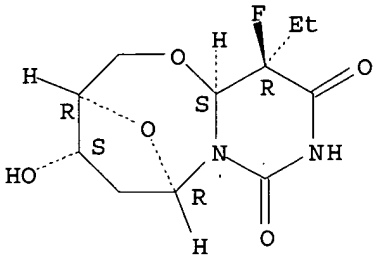
RN 475503-22-1 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 11-fluorohexahydro-11-methyl-, (3S,6R,11R,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



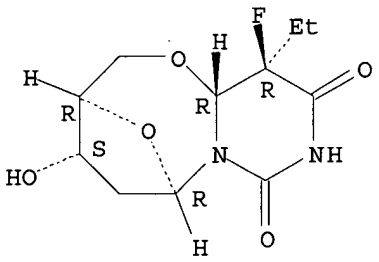
RN 475503-23-2 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 11-ethyl-11-fluorohexahydro-4-hydroxy-, (3R,4S,6R,11R,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



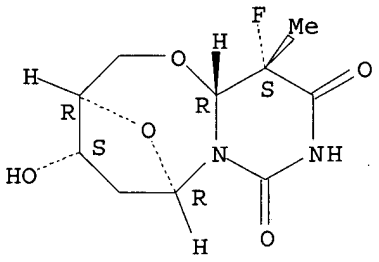
RN 475503-24-3 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 11-ethyl-11-fluorohexahydro-4-hydroxy-, (3R,4S,6R,11R,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



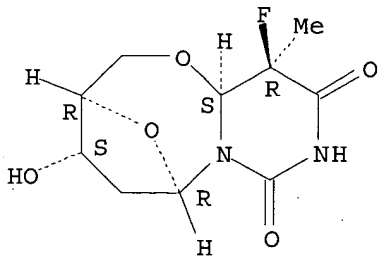
RN 475503-25-4 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 11-fluorohexahydro-4-hydroxy-11-methyl-, (3R,4S,6R,11S,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



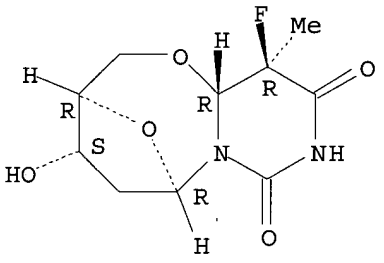
RN 475503-26-5 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 11-fluorohexahydro-4-hydroxy-11-methyl-, (3R,4S,6R,11R,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



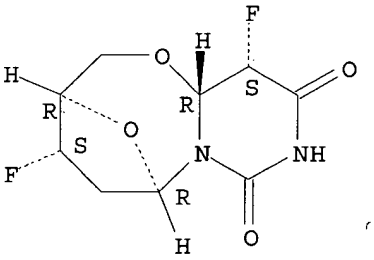
RN 475503-27-6 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 11-fluorohexahydro-4-hydroxy-11-methyl-, (3R,4S,6R,11R,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



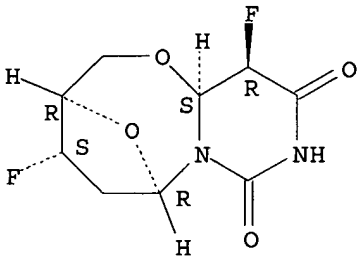
RN 475503-28-7 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 4,11-difluorohexahydro-, (3R,4S,6R,11S,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



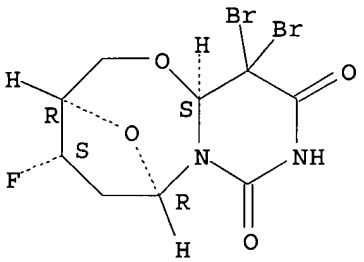
RN 475503-29-8 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 4,11-difluorohexahydro-, (3R,4S,6R,11R,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



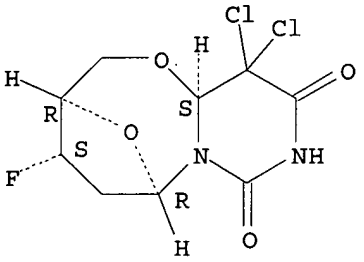
RN 475503-30-1 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 11,11-dibromo-4-fluorohexahydro-, (3R,4S,6R,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



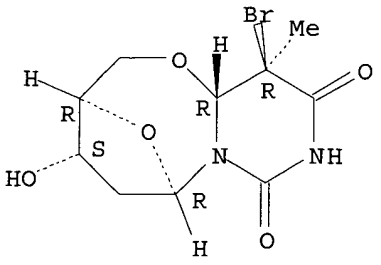
RN 475503-31-2 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 11,11-dichloro-4-fluorohexahydro-, (3R,4S,6R,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 475991-46-9 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 11-bromohexahydro-4-hydroxy-11-methyl-, (3R,4S,6R,11R,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

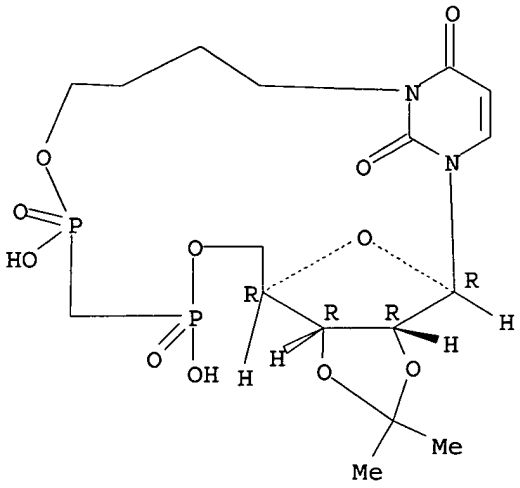


L89 ANSWER 56 OF 84 USPATFULL on STN
ACCESSION NUMBER: 2004:234004 USPATFULL
TITLE: Tetraphosphonate bicyclic trisanhydrides
INVENTOR(S): Pankiewicz, Krzysztof W., Gaithersburg, MD, UNITED STATES
Lesiak, Krystyna, Gaithersburg, MD, UNITED STATES
Watanabe, Kyoichi A., Gaithersburg, MD, UNITED STATES
PATENT ASSIGNEE(S): Pharmasset, Ltd. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004181078	A1	20040916
APPLICATION INFO.:	US 2004-812214	A1	20040329 (10)

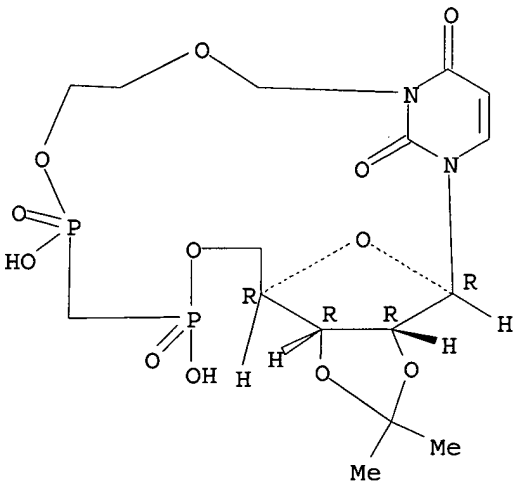
RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-8572, filed on 13 Nov 2001, GRANTED, Pat. No. US 6713623 Continuation of Ser. No. US 1997-949180, filed on 10 Oct 1997, GRANTED, Pat. No. US 6326490
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: KING & SPALDING LLP, 191 PEACHTREE STREET, N.E., ATLANTA, GA, 30303-1763
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
LINE COUNT: 3721
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are novel bicyclic tris(anhydride)s useful as intermediates in the synthesis of biologically active compounds, and the compounds which may be synthesized from such intermediates.
IT **206544-46-9P 206544-53-8P 206647-82-7P 206647-83-8P**
(preparation of nucleotide tetraphosphonate bicyclic trisanhydrides)
RN 206544-46-9 USPATFULL
CN Uridine, 3-[4-[[hydroxy(phosphonomethyl)phosphinyl]oxy]butyl]-2',3'-O-(1-methylethylidene)-, intramol. P'→5'-ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



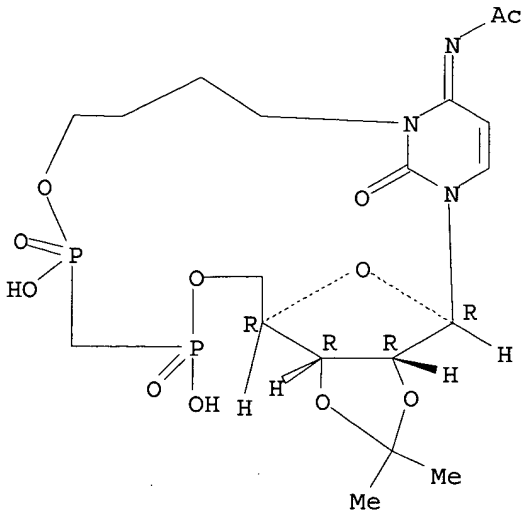
RN 206544-53-8 USPATFULL
CN Uridine, 2',3'-O-(1-methylethylidene)-3-(6,8,8-trihydroxy-6,8-dioxido-2,5-dioxa-6,8-diphosphaoct-1-yl)-, intramol. P'→5'-ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



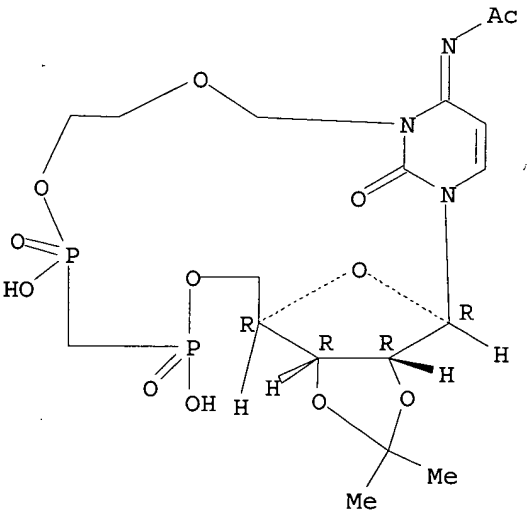
RN 206647-82-7 USPATFULL
CN Cytidine, N-acetyl-3-[4-[[hydroxy(phosphonomethyl)phosphinyl]oxy]butyl]-2',3'-O-(1-methylethylidene)-, intramol. P'→5'-ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 206647-83-8 USPATFULL
CN Cytidine, N-acetyl-2',3'-O-(1-methylethylidene)-3-(6,8,8-trihydroxy-6,8-dioxido-2,5-dioxa-6,8-diphosphaoct-1-yl)-, intramol. P'→5'-ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



L89 ANSWER 57 OF 84 USPATFULL on STN
ACCESSION NUMBER: 2003:271466 USPATFULL
TITLE: Nucleic acid derivatives
INVENTOR(S): Segev, David, Mazkeret Batya, ISRAEL
PATENT ASSIGNEE(S): Bio-Rad Laboratories Inc. (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003191074	A1	20031009	
APPLICATION INFO.:	US 2002-57928	A1	20020129	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-264308P	20010129 (60)

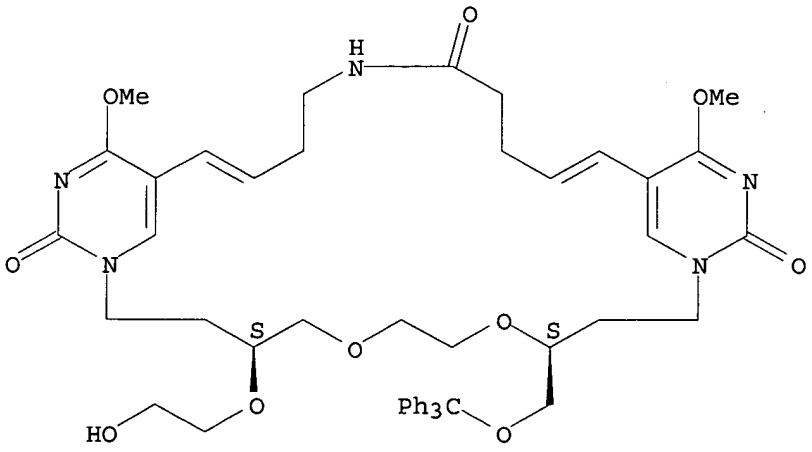
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: G.E. EHRLICH (1995) LTD., c/o ANTHONY CASTORINA, SUITE 207, 2001 JEFFERSON DAVIS HIGHWAY, ARLINGTON, VA, 22202
NUMBER OF CLAIMS: 102
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 33 Drawing Page(s)
LINE COUNT: 2941
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A compound which comprises a backbone having a plurality of chiral carbon atoms, the backbone bearing a plurality of ligands each being individually bound to a chiral carbon atom of the plurality of chiral carbon atoms, the ligands including one or more pair(s) of adjacent ligands each containing a moiety selected from the group consisting of a naturally occurring nucleobase and a nucleobase binding group, wherein moieties of the one or more pair(s) are directly linked to one another via a linker chain; building blocks for synthesizing the compound; and rises of the compound, particularly in antisense therapy.

IT **445377-76-4P 445377-77-5P**
(oligonucleotide analogs containing linked bases, methods for their synthesis, and their use in modulating gene expression and treatment of diseases)

RN 445377-76-4 USPATFULL
CN 20,23-Dioxa-6,14,16,28,30-pentaazatricyclo[26.3.1.112,16]tritriaconta-1(32),2,10,12(33),13,30-hexaene-7,15,29-trione, 25-(2-hydroxyethoxy)-13,31-dimethoxy-19-[(triphenylmethoxy)methyl]-, (19S,25S)- (9CI) (CA INDEX NAME)

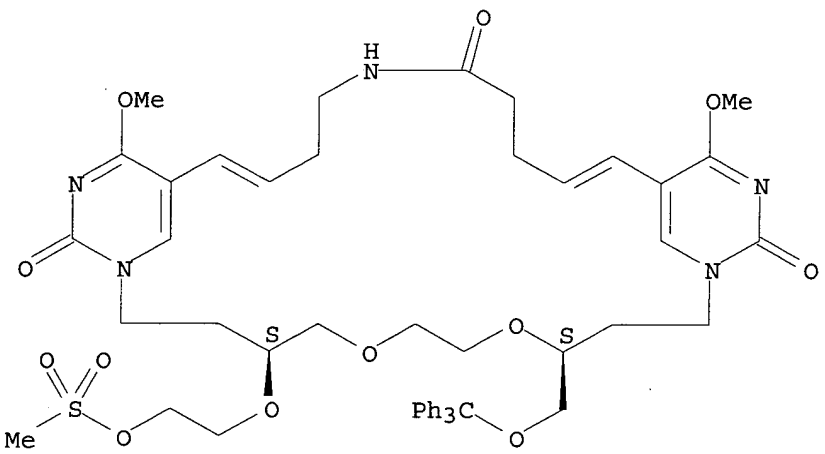
Absolute stereochemistry.
Double bond geometry unknown.



RN 445377-77-5 USPATFULL
CN 20,23-Dioxa-6,14,16,28,30-pentaazatricyclo[26.3.1.112,16]tritriaconta-1(32),2,10,12(33),13,30-hexaene-7,15,29-trione, 13,31-dimethoxy-25-[2-[(methylsulfonyl)oxy]ethoxy]-19-[(triphenylmethoxy)methyl]-, (19S,25S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



L89 ANSWER 58 OF 84 USPATFULL on STN

ACCESSION NUMBER:	2002:288348 USPATFULL
TITLE:	Tetraphosphonate bicyclic trisanhydrides
INVENTOR(S):	Pankiewicz, Krzysztof W., Gaithersburg, MD, UNITED STATES Lesiak, Krystyna, Gaithersburg, MD, UNITED STATES Watanabe, Kyoichi A., Gaithersburg, MD, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002161220	A1	20021031
	US 6713623	B2	20040330
APPLICATION INFO.:	US 2001-8572	A1	20011113 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1997-949180, filed on 10 Oct 1997, GRANTED, Pat. No. US 6326490

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-28154P	19961009 (60)
	US 1997-38360P	19970213 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	KING & SPALDING, 191 PEACHTREE STREET, N.E., ATLANTA, GA, 30303-1763
NUMBER OF CLAIMS:	26
EXEMPLARY CLAIM:	1
LINE COUNT:	3712

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are novel bicyclic tris(anhydride)s useful as intermediates in the synthesis of biologically active compounds, and the compounds which may be synthesized from such intermediates.

IT **206544-46-9P 206544-53-8P 206647-82-7P**
206647-83-8P
(preparation of nucleotide tetraphosphonate bicyclic trisanhydrides)

RN 206544-46-9 USPATFULL

CN Uridine, 3-[4-[[hydroxy(phosphonomethyl)phosphinyl]oxy]butyl]-2',3'-O-(1-methylethylidene)-, intramol. P'→5'-ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

```
=> fil lreg
FILE 'LREGISTRY' ENTERED AT 13:47:03 ON 19 MAY 2005
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LREGISTRY IS A STATIC LEARNING FILE

NEW CAS INFORMATION USE POLICIES, ENTER HELP USAGETERMS FOR DETAILS.

=> fil reg
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   18 MAY 2005  HIGHEST RN 850688-83-4
DICTIONARY FILE UPDATES:  18 MAY 2005  HIGHEST RN 850688-83-4

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> fil zcap
FILE 'ZCAPLUS' ENTERED AT 13:47:15 ON 19 MAY 2005
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strictly prohibited.

FILE COVERS 1907 - 19 May 2005 VOL 142 ISS 21
FILE LAST UPDATED: 18 May 2005 (20050518/ED)

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=> fil hcap
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FILE COVERS 1907 - 19 May 2005 VOL 142 ISS 21
FILE LAST UPDATED: 18 May 2005 (20050518/ED)

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=> fil casreact
FILE 'CASREACT' ENTERED AT 13:47:21 ON 19 MAY 2005
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FILE CONTENT:1840 - 15 May 2005 VOL 142 ISS 20

New CAS Information Use Policies, enter HELP USAGETERMS for details.

```
************************************************************
*                                                          *
*     CASREACT now has more than 9.2 million reactions     *
*                                                          *
************************************************************
```

Some CASREACT records are derived from the ZIC/VINITI database (1974-1991) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance

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=> fil toxcenter
FILE 'TOXCENTER' ENTERED AT 13:47:26 ON 19 MAY 2005
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FILE COVERS 1907 TO 17 May 2005 (20050517/ED)

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TOXCENTER has been enhanced with new files segments and search fields.
See HELP CONTENT for more information.

TOXCENTER thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary. See http://www.nlm.nih.gov/mesh/ and http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html for a description of changes.

=> fil uspatfull
FILE 'USPATFULL' ENTERED AT 13:47:30 ON 19 MAY 2005
CA INDEXING COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 17 May 2005 (20050517/PD)
FILE LAST UPDATED: 17 May 2005 (20050517/ED)
HIGHEST GRANTED PATENT NUMBER: US6895596
HIGHEST APPLICATION PUBLICATION NUMBER: US2005102725
CA INDEXING IS CURRENT THROUGH 17 May 2005 (20050517/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 17 May 2005 (20050517/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2005

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> fil wpix
FILE 'WPIX' ENTERED AT 13:47:32 ON 19 MAY 2005

FILE LAST UPDATED: 17 MAY 2005 <20050517/UP>
MOST RECENT DERWENT UPDATE: 200531 <200531/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://thomsonderwent.com/coverage/latestupdates/ <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
GUIDES, PLEASE VISIT:
http://thomsonderwent.com/support/userguides/ <<<

>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT
DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX
FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS: http://www.thomsonderwent.com/dwpifv <<<

>>> THE CPI AND EPI MANUAL CODES HAVE BEEN REVISED FROM UPDATE 200501.
PLEASE CHECK:
http://thomsonderwent.com/support/dwpiref/reftools/classification/code-revision/
FOR DETAILS. <<<

=> fil medlin
FILE 'MEDLINE' ENTERED AT 13:47:37 ON 19 MAY 2005

FILE LAST UPDATED: 18 MAY 2005 (20050518/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP
RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> fil biosis
FILE 'BIOSIS' ENTERED AT 13:47:42 ON 19 MAY 2005

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 18 May 2005 (20050518/ED)

FILE RELOADED: 19 October 2003.

```
=> fil pascal
FILE 'PASCAL' ENTERED AT 13:47:45 ON 19 MAY 2005
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FILE LAST UPDATED: 17 MAY 2005       <20050517/UP>
FILE COVERS 1977 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE
    IN THE BASIC INDEX (/BI) FIELD  <<<

=> fil jicst
FILE 'JICST-EPLUS' ENTERED AT 13:47:49 ON 19 MAY 2005
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FILE COVERS 1985 TO 16 MAY 2005 (20050516/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED
TERM (/CT) THESAURUS RELOAD.

=> fil cancerlit
FILE 'CANCERLIT' ENTERED AT 13:47:54 ON 19 MAY 2005

 FILE COVERS 1963 TO 15 Nov 2002 (20021115/ED)

 On July 28, 2002, CANCERLIT was reloaded.  See HELP RLOAD for details.

 CANCERLIT thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2002 vocabulary.  Enter HELP THESAURUS for details.

 This file contains CAS Registry Numbers for easy and accurate substance
 identification.

=> fil lifesci
FILE 'LIFESCI' ENTERED AT 13:47:58 ON 19 MAY 2005
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FILE COVERS 1978 TO 16 May 2005 (20050516/ED)

=> fil drugu
FILE 'DRUGU' ENTERED AT 13:48:04 ON 19 MAY 2005
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FILE LAST UPDATED: 16 MAY 2005       <20050516/UP>
>>>  DERWENT DRUG FILE (SUBSCRIBER)  <<<

>>>  FILE COVERS 1983 TO DATE  <<<
>>>  THESAURUS AVAILABLE IN /CT  <<<


=> fil embase
FILE 'EMBASE' ENTERED AT 13:48:08 ON 19 MAY 2005
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 FILE COVERS 1974 TO 12 May 2005 (20050512/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.
```

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> fil scisearch
FILE 'SCISEARCH' ENTERED AT 13:48:14 ON 19 MAY 2005
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FILE COVERS 1974 TO 12 May 2005 (20050512/ED)

=> fil conf
FILE 'CONF' ENTERED AT 13:48:17 ON 19 MAY 2005
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FILE LAST UPDATED: 13 MAY 2005 <20050513/UP>
FILE COVERS 1976 TO DATE.

=> fil confsci
FILE 'CONFSCI' ENTERED AT 13:48:21 ON 19 MAY 2005
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FILE COVERS 1973 TO 18 Mar 2005 (20050318/ED)

=> fil caba
FILE 'CABA' ENTERED AT 13:48:25 ON 19 MAY 2005
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FILE COVERS 1973 TO 6 May 2005 (20050506/ED)

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The CABA file was reloaded 7 December 2003. Enter HELP RLOAD for details.

=> fil bioeng
FILE 'BIOENG' ENTERED AT 13:48:28 ON 19 MAY 2005
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FILE LAST UPDATED: 18 MAY 2005 <20050518/UP>
FILE COVERS 1960 TO DATE

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=> fil biotechno
FILE 'BIOTECHNO' ENTERED AT 13:48:35 ON 19 MAY 2005
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FILE LAST UPDATED: 7 JAN 2004 <20040107/UP>
FILE COVERS 1980 TO 2003.

>>> BIOTECHNO IS NO LONGER BEING UPDATED AS OF 2004 <<<

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN /CT AND BASIC INDEX <<<

=> fil biotechds
FILE 'BIOTECHDS' ENTERED AT 13:48:41 ON 19 MAY 2005
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FILE LAST UPDATED: 13 MAY 2005 <20050513/UP>

>>> USE OF THIS FILE IS LIMITED TO BIOTECH SUBSCRIBERS <<<

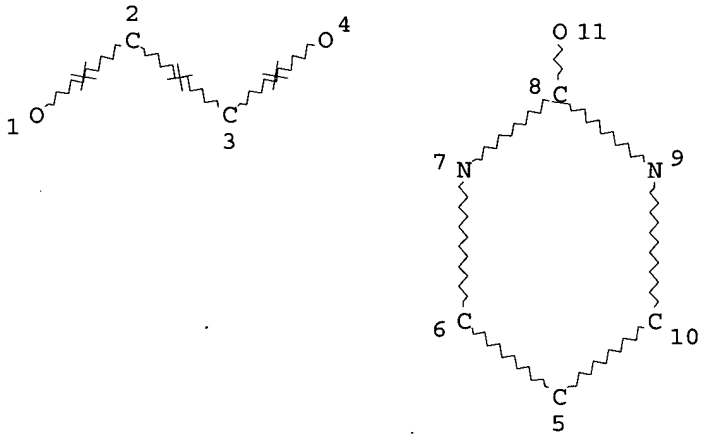
>>> NEW CLASSIFICATION SYSTEM FROM 2002 ONWARDS - SEE HELP CLA <<<

>>> NEW DISPLAY FIELDS LS AND LS2 (LEGAL STATUS DATA FROM
THE INPADOC DATABASE) AVAILABLE - SEE NEWS <<<

=> file stnguide
FILE 'STNGUIDE' ENTERED AT 13:48:45 ON 19 MAY 2005

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 13, 2005 (20050513/UP).

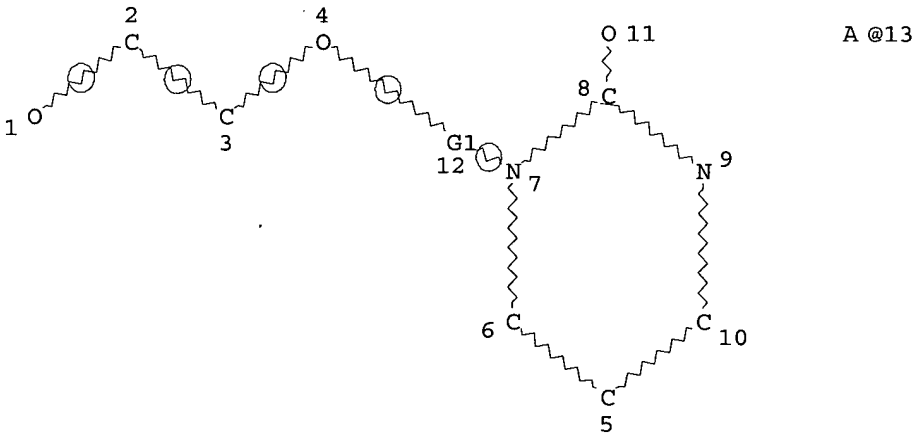
=> d que l44
L6 STR



NODE ATTRIBUTES:
NSPEC IS RC AT 1
NSPEC IS RC AT 2
NSPEC IS RC AT 3
NSPEC IS RC AT 4
CONNECT IS E2 RC AT 1
CONNECT IS E2 RC AT 4
CONNECT IS E1 RC AT 11
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE
L8 139039 SEA FILE=REGISTRY SSS FUL L6
L12 STR



REP G1=(0-20) 13
NODE ATTRIBUTES:
NSPEC IS R AT 1
NSPEC IS R AT 2

```
NSPEC   IS R       AT   3
NSPEC   IS R       AT   4
NSPEC   IS R       AT  13
CONNECT IS E2  RC AT   1
CONNECT IS E2  RC AT   4
CONNECT IS E1  RC AT  11
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  13

STEREO ATTRIBUTES: NONE
L14          962 SEA FILE=REGISTRY SUB=L8 SSS FUL L12
L17          419 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14
L21              QUE  ABB=ON  PLU=ON  ?EXPRES? OR ?TRANSCRI? OR ?TRANSLA?
L22            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17 (L) (?GENE? (5A) L21)
L23        15503 SEA FILE=HCAPLUS ABB=ON  PLU=ON  POLYNUCLEOTIDES+PFT,NT/CT
L24         4341 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "NUCLEOTIDES (L) POLY-"+PFT,NT
                 /CT
L25        66771 SEA FILE=HCAPLUS ABB=ON  PLU=ON  OLIGONUCLEOTIDES+PFT,NT/CT
L26        20253 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "NUCLEOTIDES (L) OLIGO-"+PFT,N
                 T/CT
L27           49 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17 AND (L23 OR L24 OR L25 OR
                 L26)
L28       484923 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ?GENE? (5A) L21
L29            5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28 AND L17
L30         8670 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28 AND (L23 OR L24 OR L25 OR
                 L26)
L33         5852 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ?NUCLEO? (L) ?CHIRAL?
L34           18 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L30 AND L33
L35            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L27 AND ?CHIRAL?
L36           24 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L35 OR L22 OR L29 OR L34
L41        71237 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8
L42         4126 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L41 AND L28
L43           10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L33 AND L42
L44           26 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 OR L43


=> d que nos l54
L6               STR
L8        139039 SEA FILE=REGISTRY SSS FUL L6
L12              STR
L14          962 SEA FILE=REGISTRY SUB=L8 SSS FUL L12
L45          221 SEA FILE=REGISTRY ABB=ON  PLU=ON  L14 AND CASREACT/LC
L48           63 SEA FILE=CASREACT ABB=ON  PLU=ON  L45
L54            1 SEA FILE=CASREACT ABB=ON  PLU=ON  L48 AND ?CHIRAL?/BI,AB


=> d que nos l61
L6               STR
L8        139039 SEA FILE=REGISTRY SSS FUL L6
L12              STR
L14          962 SEA FILE=REGISTRY SUB=L8 SSS FUL L12
L21              QUE  ABB=ON  PLU=ON  ?EXPRES? OR ?TRANSCRI? OR ?TRANSLA?
L46          110 SEA FILE=REGISTRY ABB=ON  PLU=ON  L14 AND TOXCENTER/LC
L55           54 SEA FILE=TOXCENTER ABB=ON  PLU=ON  L46
L56            1 SEA FILE=TOXCENTER ABB=ON  PLU=ON  L55 AND ?CHIRAL?
L57           29 SEA FILE=TOXCENTER ABB=ON  PLU=ON  L55 AND ?NUCLEO?
```

```
L58          29 SEA FILE=TOXCENTER ABB=ON  PLU=ON  (L56 OR L57)
L59      184644 SEA FILE=TOXCENTER ABB=ON  PLU=ON  ?GENE? (5A) L21
L60           2 SEA FILE=TOXCENTER ABB=ON  PLU=ON  L55 AND L59
L61          31 SEA FILE=TOXCENTER ABB=ON  PLU=ON  L58 OR L60


=> d que nos l62
L6               STR
L8       139039 SEA FILE=REGISTRY SSS FUL L6
L12              STR
L14         962 SEA FILE=REGISTRY SUB=L8 SSS FUL L12
L47          45 SEA FILE=REGISTRY ABB=ON  PLU=ON  L14 AND USPATFULL/LC
L62          10 SEA FILE=USPATFULL ABB=ON  PLU=ON  L47


=> d que l78
L63         365 SEA FILE=WPIX ABB=ON  PLU=ON  (?NUCLEO? (L) ?CHIRAL?)/BIX
L64       35754 SEA FILE=WPIX ABB=ON  PLU=ON  ?GENE?/BIX (5A) (?EXPRES?/BIX OR
                ?TRANSCRI?/BIX OR ?TRANSLA?/BIX)
L65       14875 SEA FILE=WPIX ABB=ON  PLU=ON  C07D403?/IPC
L66         470 SEA FILE=WPIX ABB=ON  PLU=ON  C07D498-18/IPC
L71         110 SEA FILE=WPIX ABB=ON  PLU=ON  L64 AND (L65 OR L66)
L72           2 SEA FILE=WPIX ABB=ON  PLU=ON  L71 AND L63
L73           3 SEA FILE=WPIX ABB=ON  PLU=ON  L71 AND ?CHIRAL?
L74          73 SEA FILE=WPIX ABB=ON  PLU=ON  L64 AND ?CHIRAL?
L75       12042 SEA FILE=WPIX ABB=ON  PLU=ON  (B04-C03C OR C04-C03C)/MC
L76           1 SEA FILE=WPIX ABB=ON  PLU=ON  L71 AND L75
L77           4 SEA FILE=WPIX ABB=ON  PLU=ON  L74 AND L75
L78           6 SEA FILE=WPIX ABB=ON  PLU=ON  L72 OR L73 OR L76 OR L77


=> d his l85

     (FILE 'MEDLINE, BIOSIS, PASCAL, JICST-EPLUS, CANCERLIT, LIFESCI, CABA,
     BIOENG, BIOTECHNO, BIOTECHDS, EMBASE, DRUGU, SCISEARCH' ENTERED AT
     13:18:23 ON 19 MAY 2005)
L85          19 DUP REM L83 (12 DUPLICATES REMOVED)

=> d que l85
L21              QUE  ABB=ON  PLU=ON  ?EXPRES? OR ?TRANSCRI? OR ?TRANSLA?
L79              QUE  ABB=ON  PLU=ON  ?POLYETH? OR ?POLYTHIOETH? OR ?PHOSP
                 HO? OR (?POLY(1W)(ETH? OR THIO?)) OR ?PHOSPHO?
L80     2708486 SEA ?GENE? (5A) L21
L81      127825 SEA ?NUCLEO? (15A) (L79 OR PEG)
L82         723 SEA L81 (L) ?CHIRAL?
L83          31 SEA L80 AND L82
L85          19 DUP REM L83 (12 DUPLICATES REMOVED)


=> dup rem l44 l54 l61 l62 l78 l85
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PROCESSING COMPLETED FOR L61
PROCESSING COMPLETED FOR L62
PROCESSING COMPLETED FOR L78
PROCESSING COMPLETED FOR L85
L89 84 DUP REM L44 L54 L61 L62 L78 L85 (9 DUPLICATES REMOVED)
ANSWERS '1-26' FROM FILE HCAPLUS
ANSWERS '27-54' FROM FILE TOXCENTER
ANSWERS '55-64' FROM FILE USPATFULL
ANSWERS '65-69' FROM FILE WPIX
ANSWER '70' FROM FILE BIOSIS
ANSWERS '71-72' FROM FILE CANCERLIT
ANSWERS '73-74' FROM FILE BIOTECHNO
ANSWERS '75-82' FROM FILE BIOTECHDS
ANSWERS '83-84' FROM FILE SCISEARCH

=> d ibib ed ab hitind hitstr

L89 ANSWER 1 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:430908 HCAPLUS
DOCUMENT NUMBER: 141:17622
TITLE: Preparation of 2'-fluoro substituted oligoribonucleotides and compositions for use in treatment of obesity and diabetes
INVENTOR(S): Allerson, Charles; Bhat, Balkrishen; Eldrup, Anne B.; Manoharan, Muthiah; Griffey, Richard H.; Baker, Brenda F.; Swayze, Eric E.
PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 40
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004044136	A2	20040527	WO 2003-US35071	20031104
WO 2004044136	A3	20050224		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-423760P P 20021105
ED Entered STN: 27 May 2004
AB The present invention provides methods for preparation of 2'-fluoro substituted oligoribonucleotides and compns. for use in treatment of obesity and diabetes. The compns. are useful for targeting selected nucleic acid mols. and modulating the **expression** of one or more **genes**. In preferred embodiments the compns. of the present invention hybridize to a portion of a target RNA resulting in loss of normal function of the target RNA.
IC ICM C12N
CC 1-10 (Pharmacology)
Section cross-reference(s): 3
IT **Antisense oligonucleotides**
Oligonucleotides
RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2'-fluoro substituted oligoribonucleotides and compns. for use in treatment of obesity and diabetes)
IT 13598-36-2, Phosphonic acid 19073-37-1, Phosphorodithioate
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**chiral**, as **internucleoside** linking group; preparation of 2'-fluoro substituted **oligoribonucleotides** and compns. for use in treatment of obesity and diabetes)

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=> file stnguide
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 13, 2005 (20050513/UP).

=> d ibib ed ab hitind hitstr 2-26
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, TOXCENTER, USPATFULL, WPIX, BIOSIS,
CANCERLIT, BIOTECHNO, BIOTECHDS, SCISEARCH' - CONTINUE? (Y)/N:y


L89  ANSWER 2 OF 84  HCAPLUS  COPYRIGHT 2005 ACS on STN DUPLICATE 2
ACCESSION NUMBER:        2003:883463  HCAPLUS
DOCUMENT NUMBER:         140:124597
TITLE:                   Ultraviolet radiation-induced DNA damage in promoter
                         elements inhibits gene expression
AUTHOR(S):               Ghosh, Rita; Tummala, Ramakumar; Mitchell, David L.
CORPORATE SOURCE:        Department of Cancer Causation and Prevention, AMC
                         Cancer Research Centre, University of Colorado,
                         Denver, CO, 80214, USA
SOURCE:                  FEBS Letters (2003), 554(3), 427-432
                         CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER:               Elsevier Science B.V.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
ED   Entered STN:  11 Nov 2003
AB   Repair of DNA damage in gene promoters is slower than in actively
     transcribed genes.  Persistent damage in gene promoters
     though transient can have significant biol. effects on regulated
     gene expression.  In this study we investigated the
     effect of UV radiation on gene promoter-associated functions when DNA damage
     is located within and outside transcription factor binding sites.  Our
     results show that both cyclobutane pyrimidine dimers and (6-4)
     photoproducts inhibit DNA-protein interaction, in vitro transcript
     production and transactivation of reporter genes.  The biol.
     significance of transient DNA damage as a mechanism in carcinogenesis is
     discussed.
CC   8-10 (Radiation Biochemistry)
     Section cross-reference(s): 14
ST   UV DNA damage promoter element gene expression
     carcinogenesis
IT   Transcription factors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (NF-κB (nuclear factor of κ light chain gene enhancer in
        B-cells); UV-induced DNA damage in promoter elements inhibits
        gene expression)
IT   DNA repair
     UV radiation
        (UV-induced DNA damage in promoter elements inhibits gene
        expression)
IT   Promoter (genetic element)
     Reporter gene
     Transcription factors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (UV-induced DNA damage in promoter elements inhibits gene
        expression)
```

IT Pyrimidine dimers
RL: BSU (Biological study, unclassified); FMU (Formation, unclassified); BIOL (Biological study); FORM (Formation, nonpreparative)
(cyclobutane-linked; UV-induced DNA damage in promoter elements inhibits **gene expression**)

IT DNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(damage; UV-induced DNA damage in promoter elements inhibits **gene expression**)

IT **Gene**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**expression**; UV-induced DNA damage in promoter elements inhibits **gene expression**)

IT Transformation, neoplastic
(mechanism; UV-induced DNA damage in promoter elements inhibits **gene expression**)

IT Pyrimidine bases
RL: BSU (Biological study, unclassified); FMU (Formation, unclassified); BIOL (Biological study); FORM (Formation, nonpreparative)
(photoproducts; UV-induced DNA damage in promoter elements inhibits **gene expression**)

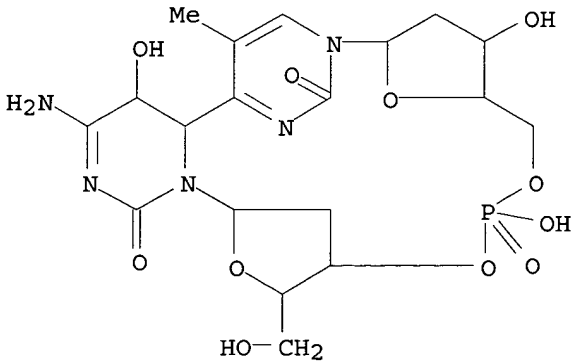
IT DNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(protein interaction; UV-induced DNA damage in promoter elements inhibits **gene expression**)

IT 33407-74-8 **145555-23-3**
RL: BSU (Biological study, unclassified); FMU (Formation, unclassified); BIOL (Biological study); FORM (Formation, nonpreparative)
(UV-induced DNA damage in promoter elements inhibits **gene expression**)

IT **145555-23-3**
RL: BSU (Biological study, unclassified); FMU (Formation, unclassified); BIOL (Biological study); FORM (Formation, nonpreparative)
(UV-induced DNA damage in promoter elements inhibits **gene expression**)

RN 145555-23-3 HCAPLUS

CN 3'-Cytidylic acid, 2'-deoxy-6-[1-(2-deoxy-β-D-erythro-pentofuranosyl)-1,2-dihydro-5-methyl-2-oxo-4-pyrimidinyl]-5,6-dihydro-5-hydroxy-, intramol. 3',5'''-ester, (5R,6S)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 3 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2002:595034 HCAPLUS
DOCUMENT NUMBER: 137:151580
TITLE: Oligonucleotide analogs containing linked bases, methods for their synthesis, and their use in modulating **gene expression** and treatment of diseases
INVENTOR(S): Segev, David
PATENT ASSIGNEE(S): Bio-Rad Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002061110	A2	20020808	WO 2002-IL83	20020129
WO 2002061110	A3	20030206		
WO 2002061110	C1	20031120		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2436665	AA	20020808	CA 2002-2436665	20020129
US 2003191074	A1	20031009	US 2002-57928	20020129
EP 1363640	A2	20031126	EP 2002-711178	20020129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004537503	T2	20041216	JP 2002-561045	20020129
PRIORITY APPLN. INFO.:			US 2001-264308P P	20010129
			WO 2002-IL83 W	20020129

OTHER SOURCE(S): MARPAT 137:151580
ED Entered STN: 09 Aug 2002
AB Nucleic acid and **oligonucleotide** analogs containing **nucleobases** attached to **chiral** carbons in the backbone and containing ≥1 paris of adjacent **nucleobases** covalently linked together are disclosed. The backbone may be a polyether, e.g., PEG, or polyether derivs. such as poly(ether-thioether), poly(ether-sulfone), and poly(ether-sulfoxide). Linked dimer building blocks and methods for their synthesis as well as methods for solution or solid phase synthesis of the oligo- and **polynucleotide** analogs are disclosed. The analogs may be used to modulate **gene expression** and to treat diseases. Thus, the solution phase and solid phase synthesis of PEG-linked oligo-T was demonstrated. The synthesis of a thymidine-linked thymidine dimer with PEG backbone was also shown.
IC ICM C12Q
CC 6-2 (General Biochemistry)
Section cross-reference(s): 1, 33
ST **oligonucleotide polynucleotide** analog **chiral** carbon polyether backbone linked base; **gene expression** modulation **oligonucleotide polynucleotide** analog
IT DNA
RNA

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(degradation of, induction of; oligonucleotide analogs containing linked bases,
methods for their synthesis, and their use in modulating **gene expression** and treatment of diseases)

IT **Gene**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**expression**; oligonucleotide analogs containing linked bases, methods for their synthesis, and their use in modulating **gene expression** and treatment of diseases)

IT **Transcription, genetic**
Translation, genetic
(modulation of; oligonucleotide analogs containing linked bases, methods for their synthesis, and their use in modulating **gene expression** and treatment of diseases)

IT Antiviral agents
Nucleic acid hybridization
(oligonucleotide analogs containing linked bases, methods for their synthesis, and their use in modulating **gene expression** and treatment of diseases)

IT **Oligonucleotides**
Polynucleotides
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(oligonucleotide analogs containing linked bases, methods for their synthesis, and their use in modulating **gene expression** and treatment of diseases)

IT DNA formation
(replication, modulation of; oligonucleotide analogs containing linked bases, methods for their synthesis, and their use in modulating **gene expression** and treatment of diseases)

IT 67-64-1, Acetone, reactions 71-30-7, Cytosine 100-39-0, Benzyl bromide 106-95-6, Allyl bromide, reactions 124-63-0, Methanesulfonyl chloride 591-80-0, 4-Pentenoic acid 617-55-0, (S)-(-)-Dimethyl malate 824-94-2, 4-Methoxybenzyl chloride 1710-98-1, 4-Tert-Butylbenzoyl chloride 3551-55-1, 2,4-Dimethoxypyrimidine 3587-60-8, Benzyloxymethyl chloride 166252-95-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(oligonucleotide analogs containing linked bases, methods for their synthesis, and their use in modulating **gene expression** and treatment of diseases)

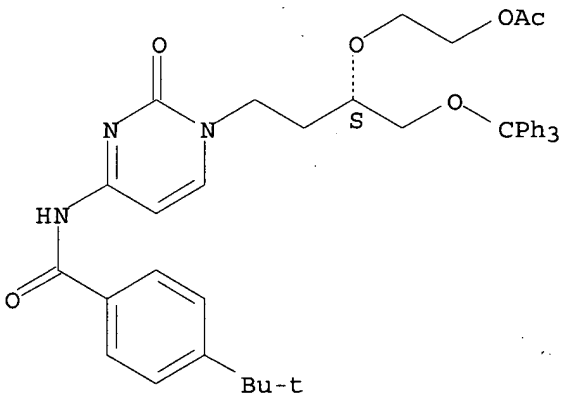
IT 818-57-5P, Methyl 4-pentenoate 3326-32-7P, Fluorescein-5-isothiocyanate 32233-43-5P 42890-76-6P 52522-99-3P 90330-19-1P 119451-90-0P 135697-25-5P 193416-58-9P 195257-54-6P 445377-33-3P 445377-34-4P 445377-35-5P 445377-36-6P 445377-37-7P **445377-38-8P** **445377-39-9P** **445377-40-2P** **445377-41-3P** **445377-42-4P** **445377-43-5P** **445377-44-6P** **445377-45-7P** **445377-46-8P** **445377-47-9P** **445377-48-0P** **445377-49-1P** **445377-50-4P** 445377-52-6DP, conjugates with Wang resin **445377-54-8DP**, conjugates with Wang resin **445377-56-0P** **445377-58-2P** **445377-60-6P** **445377-62-8P** 445377-65-1P 445377-66-2P 445377-68-4P **445377-70-8P** 445377-71-9P 445377-72-0P **445377-73-1P** **445377-74-2P** **445377-75-3P** **445377-76-4P** **445377-77-5P** 445377-78-6P 445377-79-7P **445377-80-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(oligonucleotide analogs containing linked bases, methods for their synthesis, and their use in modulating **gene**

expression and treatment of diseases)

IT **445377-38-8P 445377-39-9P 445377-40-2P**
445377-41-3P 445377-42-4P 445377-43-5P
445377-44-6P 445377-45-7P 445377-46-8P
445377-47-9P 445377-48-0P 445377-49-1P
445377-50-4P 445377-54-8DP, conjugates with Wang resin
445377-56-0P 445377-58-2P 445377-60-6P
445377-62-8P 445377-70-8P 445377-73-1P
445377-74-2P 445377-75-3P 445377-76-4P
445377-77-5P 445377-80-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(oligonucleotide analogs containing linked bases, methods for their synthesis, and their use in modulating **gene expression** and treatment of diseases)

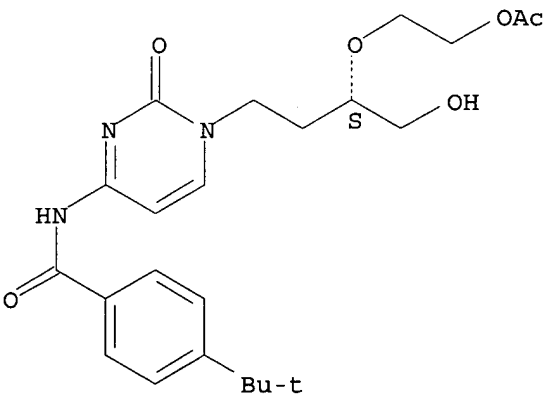
RN 445377-38-8 HCAPLUS
CN Benzamide, N-[1-[(3S)-3-[2-(acetyloxy)ethoxy]-4-(triphenylmethoxy)butyl]-1,2-dihydro-2-oxo-4-pyrimidinyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



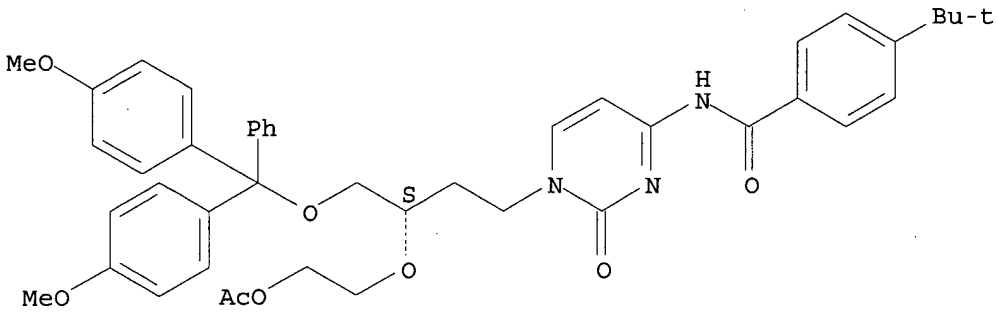
RN 445377-39-9 HCAPLUS
CN Benzamide, N-[1-[(3S)-3-[2-(acetyloxy)ethoxy]-4-hydroxybutyl]-1,2-dihydro-2-oxo-4-pyrimidinyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



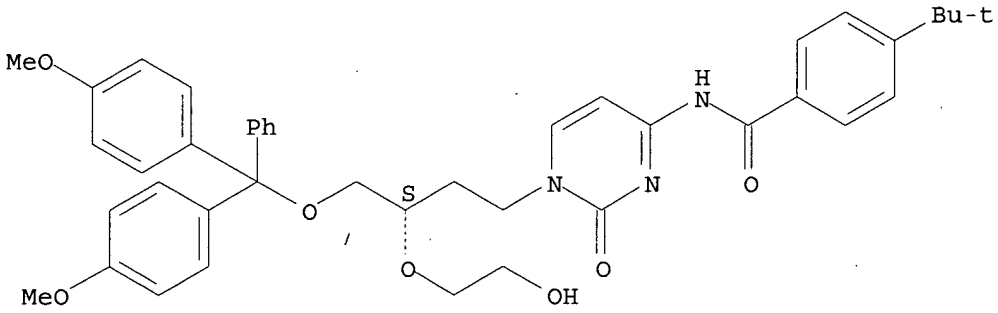
RN 445377-40-2 HCAPLUS
CN Benzamide, N-[1-[(3S)-3-[2-(acetyloxy)ethoxy]-4-[bis(4-methoxyphenyl)phenylmethoxy]butyl]-1,2-dihydro-2-oxo-4-pyrimidinyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



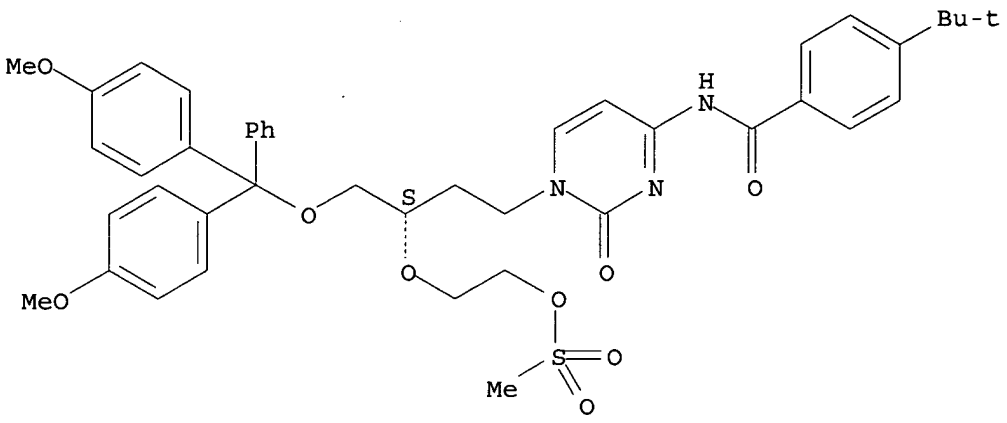
RN 445377-41-3 HCAPLUS
CN Benzamide, N-[1-[(3S)-4-[bis(4-methoxyphenyl)phenylmethoxy]-3-(2-hydroxyethoxy)butyl]-1,2-dihydro-2-oxo-4-pyrimidinyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



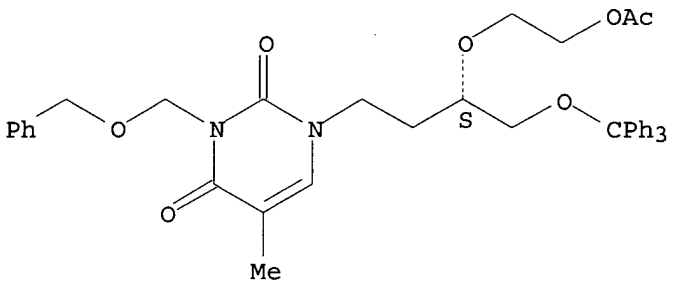
RN 445377-42-4 HCAPLUS
CN Benzamide, N-[1-[(3S)-4-[bis(4-methoxyphenyl)phenylmethoxy]-3-[2-[(methylsulfonyl)oxy]ethoxy]butyl]-1,2-dihydro-2-oxo-4-pyrimidinyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



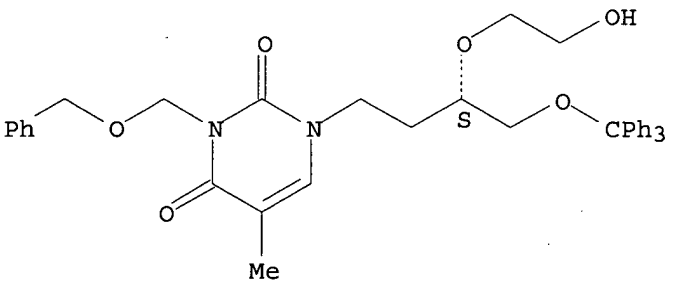
RN 445377-43-5 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(3S)-3-[2-(acetyloxy)ethoxy]-4-(triphenylmethoxy)butyl]-5-methyl-3-[(phenylmethoxy)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



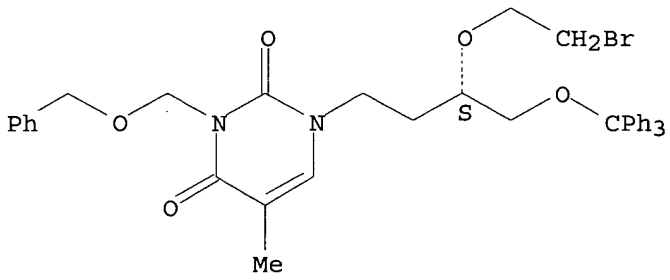
RN 445377-44-6 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(3S)-3-(2-hydroxyethoxy)-4-(triphenylmethoxy)butyl]-5-methyl-3-[(phenylmethoxy)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



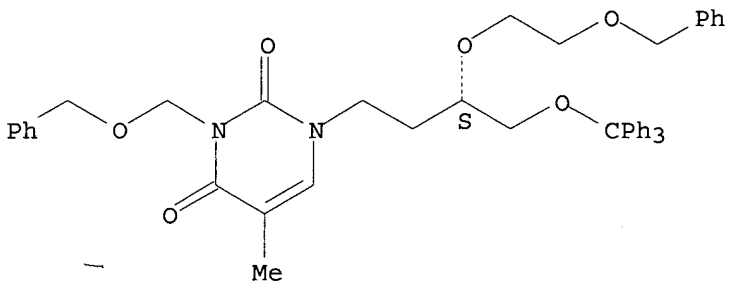
RN 445377-45-7 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(3S)-3-(2-bromoethoxy)-4-(triphenylmethoxy)butyl]-5-methyl-3-[(phenylmethoxy)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



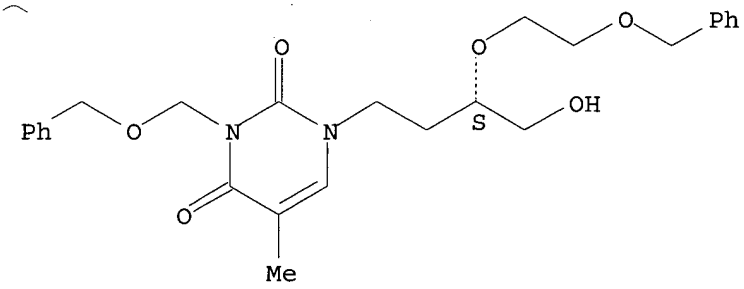
RN 445377-46-8 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-methyl-1-[(3S)-3-[2-(phenylmethoxy)ethoxy]-4-(triphenylmethoxy)butyl]-3-[(phenylmethoxy)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 445377-47-9 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(3S)-4-hydroxy-3-[2-(phenylmethoxy)ethoxy]butyl]-5-methyl-3-[(phenylmethoxy)methyl]- (9CI) (CA INDEX NAME)

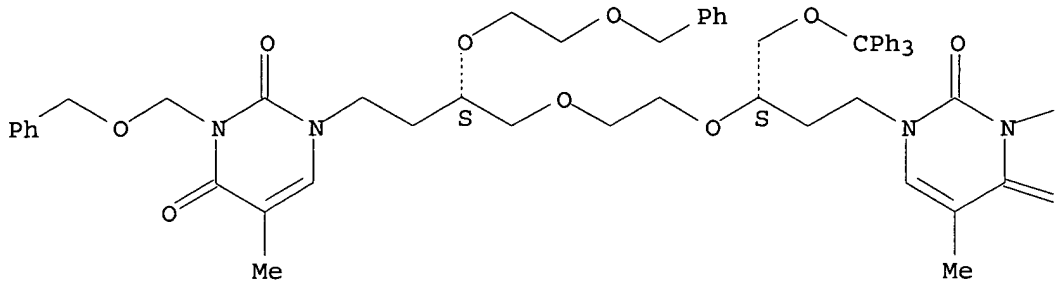
Absolute stereochemistry.



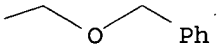
RN 445377-48-0 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(3S,9S)-9-[2-[3,4-dihydro-5-methyl-2,4-dioxo-3-[(phenylmethoxy)methyl]-1(2H)-pyrimidinyl]ethyl]-14-phenyl-3-[(triphenylmethoxy)methyl]-4,7,10,13-tetraoxatetradec-1-yl]-5-methyl-3-[(phenylmethoxy)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

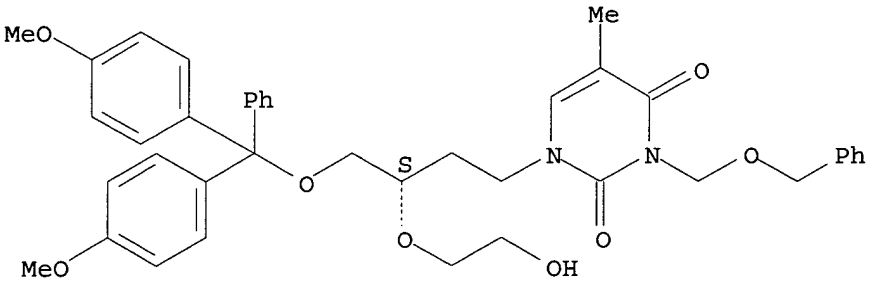


PAGE 1-B



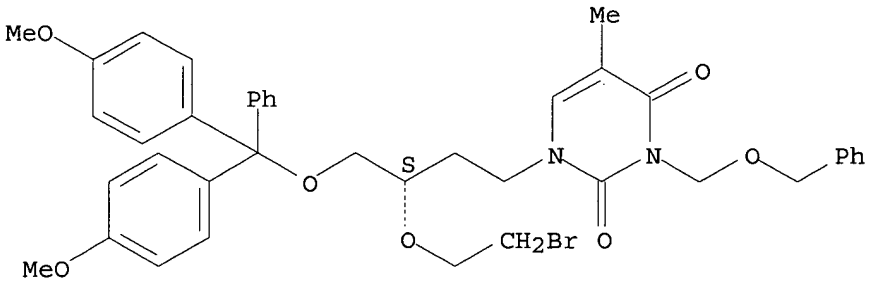
RN 445377-49-1 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(3S)-4-[bis(4-methoxyphenyl)phenylmethoxy]-3-(2-hydroxyethoxy)butyl]-5-methyl-3-[(phenylmethoxy)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 445377-50-4 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(3S)-4-[bis(4-methoxyphenyl)phenylmethoxy]-3-(2-bromoethoxy)butyl]-5-methyl-3-[(phenylmethoxy)methyl]- (9CI) (CA INDEX NAME)

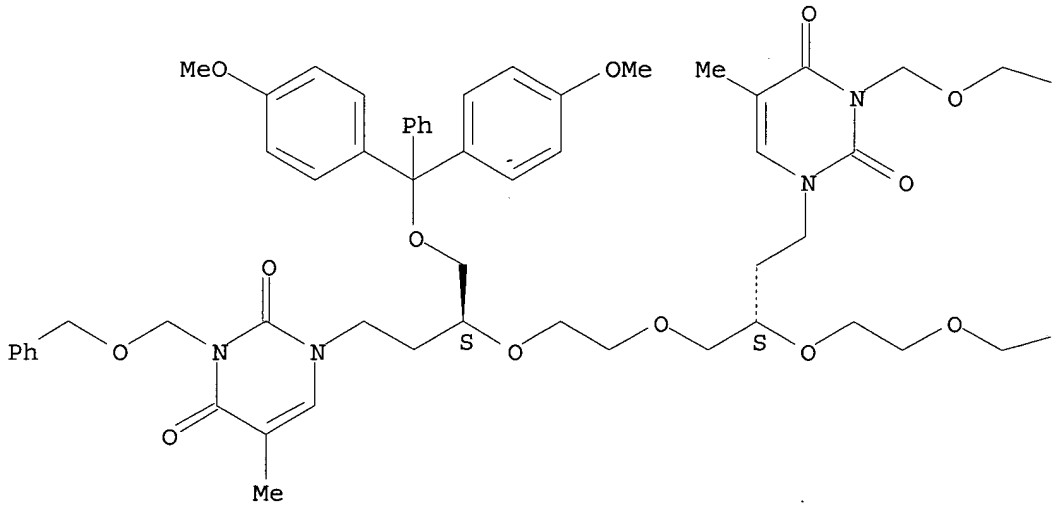
Absolute stereochemistry.



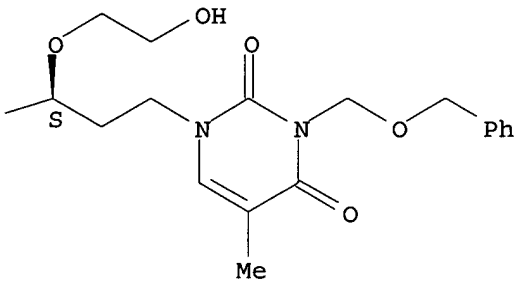
RN 445377-54-8 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1,1'-[(3S,9S,15S)-3-[[bis(4-methoxyphenyl)phenylmethoxy]methyl]-9-[2-[3,4-dihydro-5-methyl-2,4-dioxo-3-[(phenylmethoxy)methyl]-1(2H)-pyrimidinyl]ethyl]-15-(2-hydroxyethoxy)-4,7,10,13-tetraoxaheptadecane-1,17-diyl]bis[5-methyl-3-[(phenylmethoxy)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



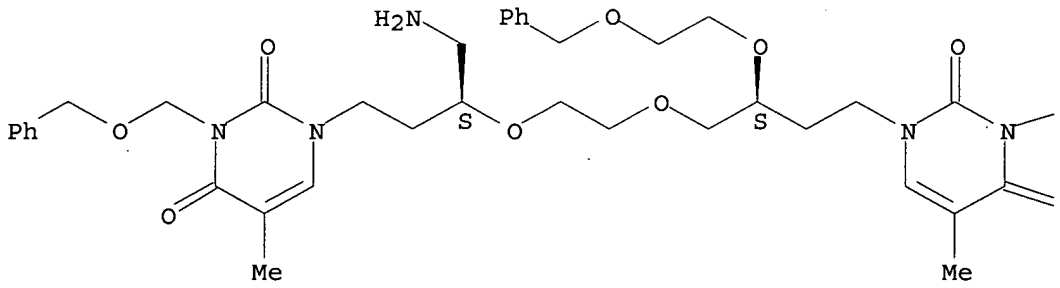
PAGE 1-B



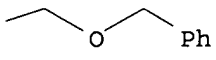
RN 445377-56-0 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(3S,9S)-3-(aminomethyl)-9-[2-[3,4-dihydro-5-methyl-2,4-dioxo-3-[(phenylmethoxy)methyl]-1(2H)-pyrimidinyl]ethyl]-14-phenyl-4,7,10,13-tetraoxatetradec-1-yl]-5-methyl-3-[(phenylmethoxy)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



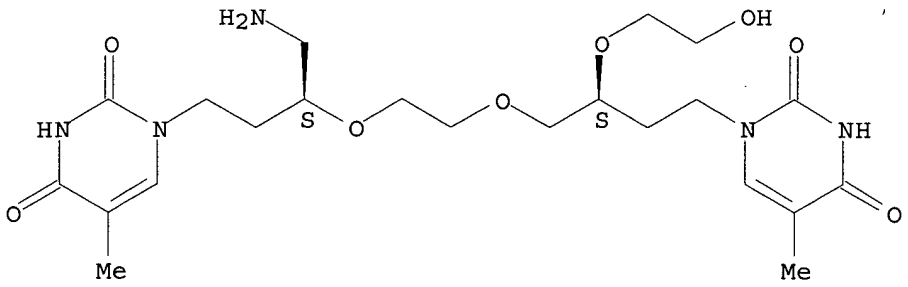
PAGE 1-B



RN 445377-58-2 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(3S)-4-amino-3-[2-[(2S)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-2-(2-hydroxyethoxy)butoxy]ethoxy]butyl

]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 445377-60-6 HCAPLUS
CN 5,8,11-Trioxa-2-azatridecanethioamide, 4,10-bis[2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethyl]-N-(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)-13-hydroxy-, (4S,10S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

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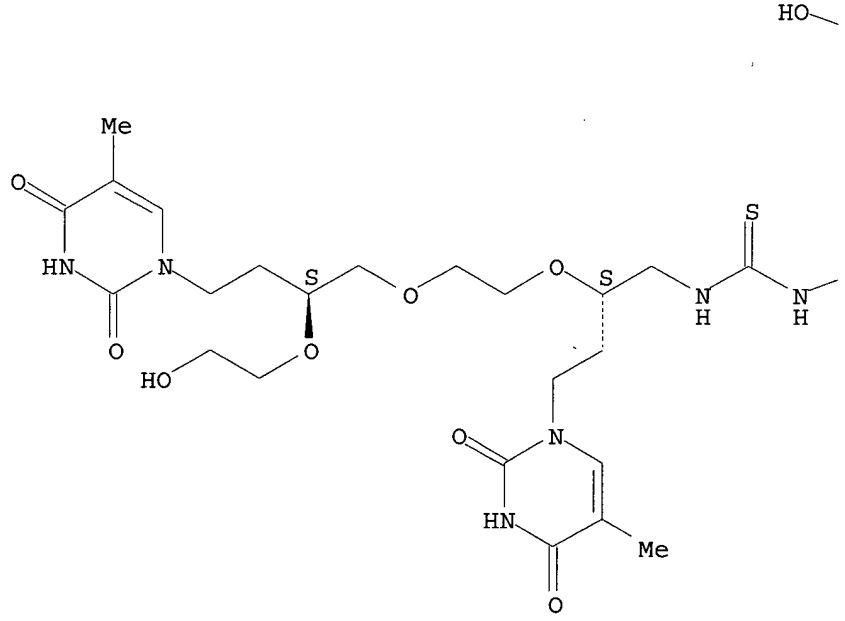
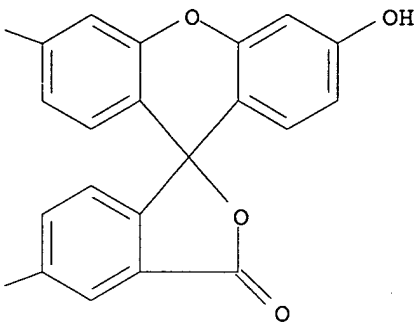


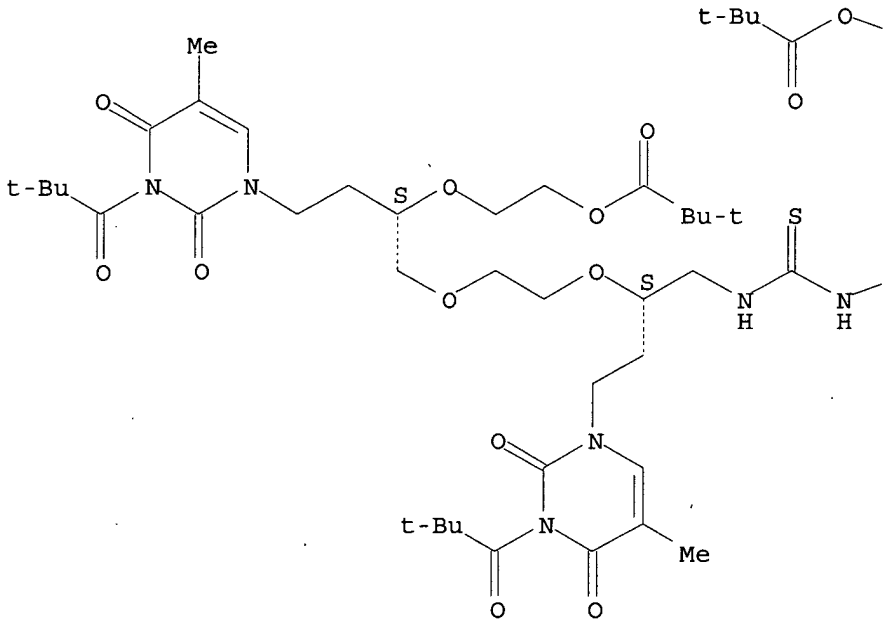
PAGE 1-B



RN 445377-62-8 HCAPLUS
CN Propanoic acid, 2,2-dimethyl-, 5-[[(4S,10S)-4,10-bis[2-[3-(2,2-dimethyl-1-oxopropyl)-3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl]ethyl]-16,16-dimethyl-15-oxo-1-thioxo-5,8,11,14-tetraoxa-2-azaheptadec-1-yl]amino]-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthene]-3',6'-diyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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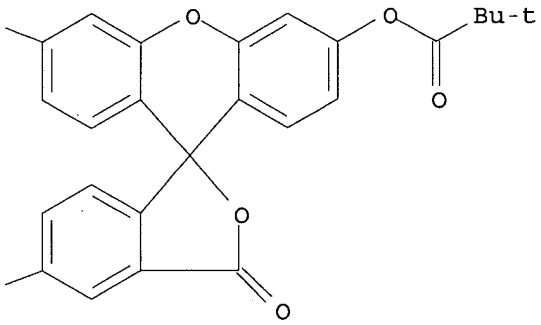
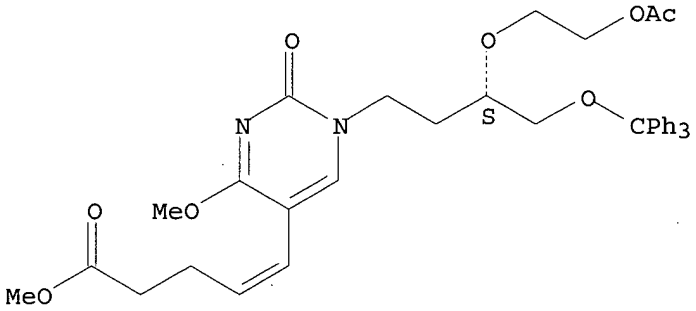


RN 445377-70-8 HCAPLUS
CN 4-Pentenoic acid, 5-[1-[(3S)-3-[2-(acetyloxy)ethoxy]-4-(triphenylmethoxy)butyl]-1,2-dihydro-4-methoxy-2-oxo-5-pyrimidinyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 445377-73-1 HCAPLUS
CN 4-Pentenoic acid, 5-[1,2-dihydro-4-methoxy-1-[(3S,9S)-9-[2-[(4-methoxyphenyl)methoxy]ethyl]-15,15-dimethyl-14-oxo-3-[(triphenylmethoxy)methyl]-4,7,10,13-tetraoxahexadec-1-yl]-2-oxo-5-pyrimidinyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

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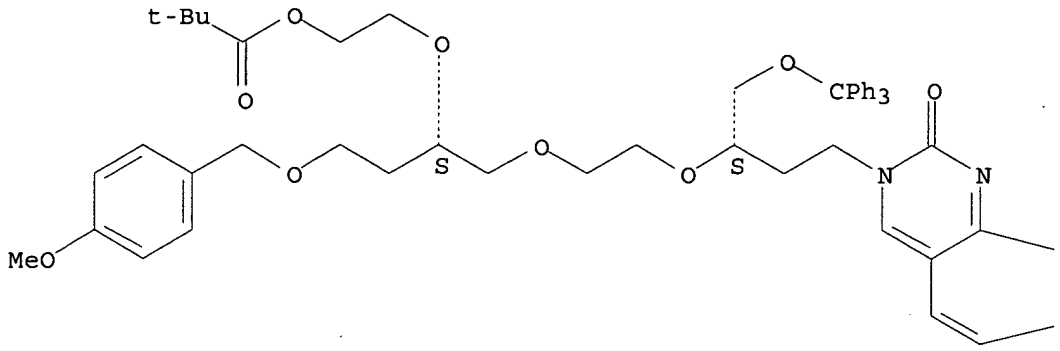

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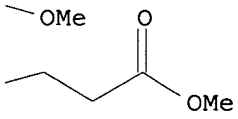
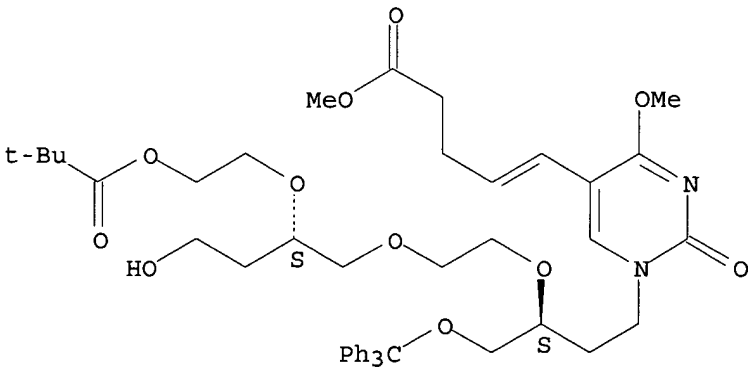


RN 445377-74-2 HCAPLUS
CN 4-Pentenoic acid, 5-[1,2-dihydro-1-[(3S,9S)-9-(2-hydroxyethyl)-15,15-dimethyl-14-oxo-3-[(triphenylmethoxy)methyl]-4,7,10,13-tetraoxahexadec-1-yl]-4-methoxy-2-oxo-5-pyrimidinyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 445377-75-3 HCAPLUS

CN 4-Pentenoic acid, 5-[1-[(3S)-3-[2-[(2S)-4-[5-(4-amino-1-butenyl)-4-methoxy-2-oxo-1(2H)-pyrimidinyl]-2-(2-hydroxyethoxy)butoxy]ethoxy]-4-(triphenylmethoxy)butyl]-1,2-dihydro-4-methoxy-2-oxo-5-pyrimidinyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

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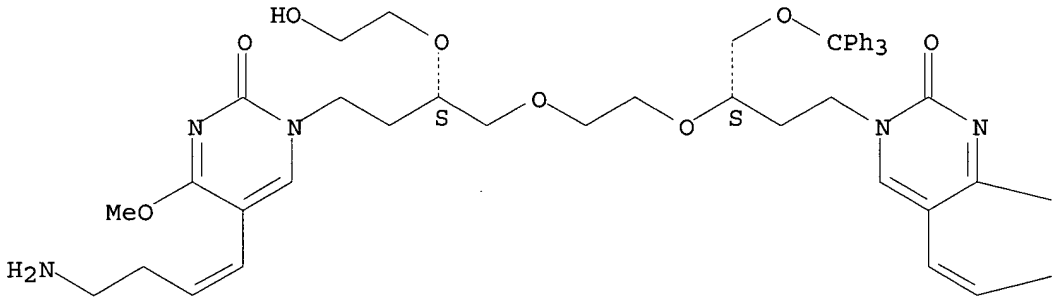

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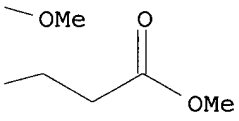
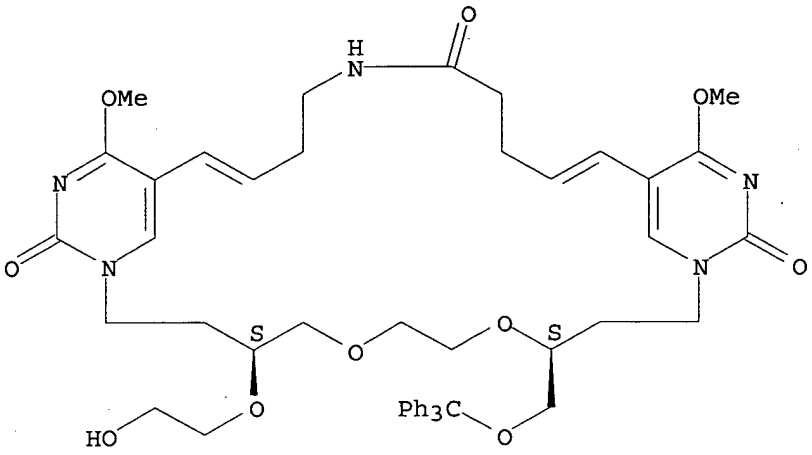


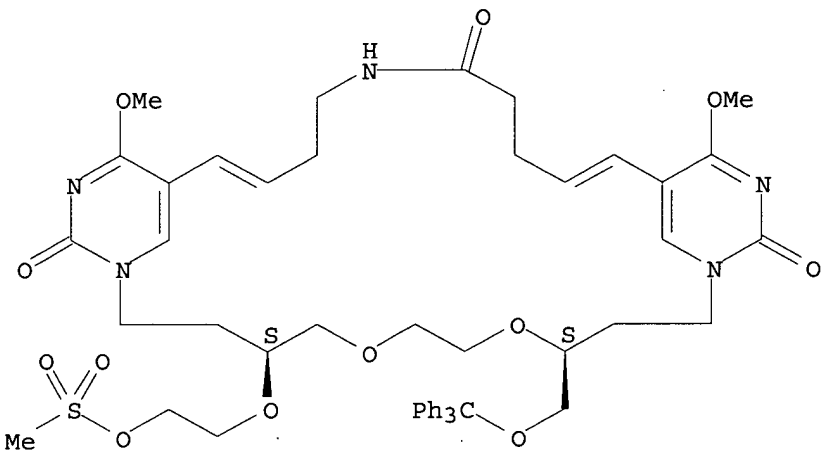
RN 445377-76-4 HCAPLUS
CN 20,23-Dioxa-6,14,16,28,30-pentaazatricyclo[26.3.1.112,16]tritriaconta-1(32),2,10,12(33),13,30-hexaene-7,15,29-trione, 25-(2-hydroxyethoxy)-13,31-dimethoxy-19-[(triphenylmethoxy)methyl]-, (19S,25S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



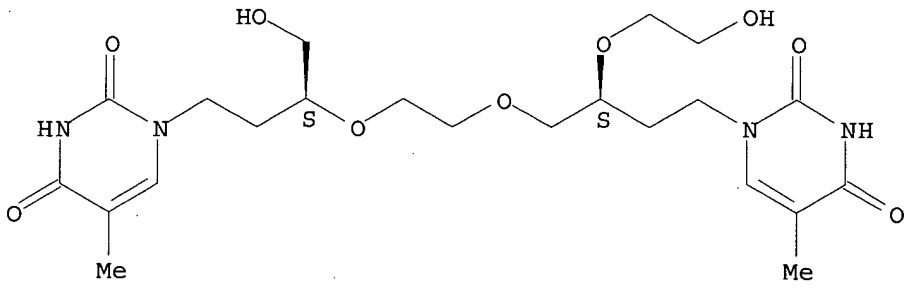
RN 445377-77-5 HCAPLUS
CN 20,23-Dioxa-6,14,16,28,30-pentaazatricyclo[26.3.1.112,16]tritriaconta-1(32),2,10,12(33),13,30-hexaene-7,15,29-trione, 13,31-dimethoxy-25-[2-[(methylsulfonyl)oxy]ethoxy]-19-[(triphenylmethoxy)methyl]-, (19S,25S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 445377-80-0 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(3S)-3-[2-[(2S)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-2-(2-hydroxyethoxy)butoxy]ethoxy]-4-hydroxybutyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 4 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2000:626421 HCAPLUS
DOCUMENT NUMBER: 133:350458
TITLE: Synthesis and Properties of Oligonucleotides Having a Phosphorus **Chiral** Center by Incorporation of Conformationally Rigid 5'-Cyclouridylic Acid Derivatives
AUTHOR(S): Sekine, Mitsuo; Kurasawa, Osamu; Shohda, Koh-ichiroh; Seio, Kohji; Wada, Takeshi
CORPORATE SOURCE: Department of Life Science, Tokyo Institute of Technology, Midoriku Yokohama, 226-8501, Japan
SOURCE: Journal of Organic Chemistry (2000), 65(20), 6515-6524
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:350458
ED Entered STN: 10 Sep 2000
AB This paper describes the design and synthesis of a conformationally rigid dimer building block Umpc3Um as a **chiral** center at the phosphate group with the S/N junction where c3 refers to a propylene bridge linked between the uracil 5-position and 5'-phosphate group of pUm. The extensive H1 NMR anal. of Umpc3Um suggests that the 5'-upstream Um has predominantly a C2'-endo conformation and the pc3Um moiety exists almost exclusively in a C3'-endo conformation. The absolute configuration of the diastereomers Umpc3Um was determined by CD spectroscopy as well as computer simulations. The Tm expts. of the duplexes formed between these modified oligomers and the complementary oligomers imply that the modified oligomer having Umpc3Um(fast) has the Sp configuration at the **chiral** phosphoryl group.
CC 33-10 (Carbohydrates)
Section cross-reference(s): 22
IT **Oligodeoxyribonucleotides**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(duplexes; synthesis and properties of oligonucleotides having a phosphorus **chiral** center by incorporation of conformationally rigid 5'-cyclouridylic acid derivs.)
IT Absolute configuration
(synthesis and properties of oligonucleotides having a phosphorus **chiral** center by incorporation of conformationally rigid 5'-cyclouridylic acid derivs.)
IT **Oligonucleotides**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(synthesis and properties of oligonucleotides having a phosphorus **chiral** center by incorporation of conformationally rigid 5'-cyclouridylic acid derivs.)

IT **305366-02-3P 305366-03-4P 305366-06-7P**
305366-07-8P 305872-67-7P 305872-68-8P 305872-69-9P
305872-70-2P 306329-85-1P 306329-86-2P 306329-87-3P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(synthesis and properties of oligonucleotides having a phosphorus **chiral** center by incorporation of conformationally rigid 5'-cyclouridylic acid derivs.)

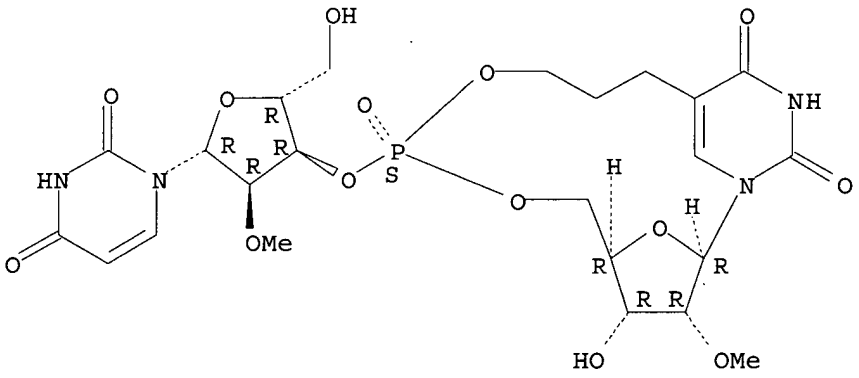
IT 74405-40-6D, polymer support 103285-22-9 119702-12-4D, polymer support 287101-04-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and properties of oligonucleotides having a phosphorus **chiral** center by incorporation of conformationally rigid 5'-cyclouridylic acid derivs.)

IT 110764-79-9P **305365-98-4P 305365-99-5P**
305366-00-1P 305366-01-2P 305366-04-5P
305366-05-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and properties of oligonucleotides having a phosphorus **chiral** center by incorporation of conformationally rigid 5'-cyclouridylic acid derivs.)

IT **305366-02-3P 305366-03-4P 305366-06-7P**
305366-07-8P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(synthesis and properties of oligonucleotides having a phosphorus **chiral** center by incorporation of conformationally rigid 5'-cyclouridylic acid derivs.)

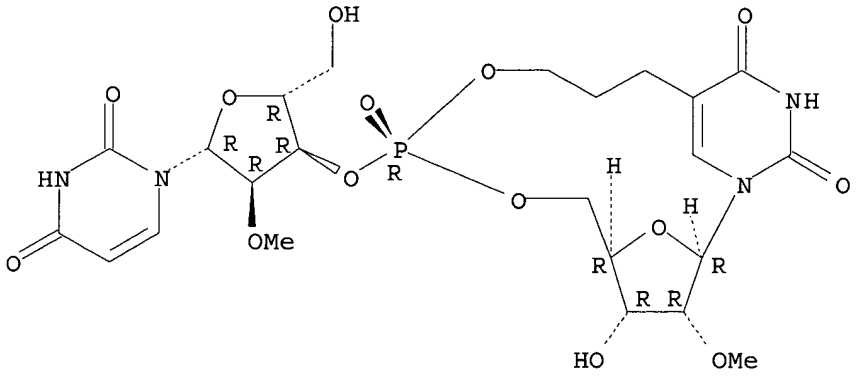
RN 305366-02-3 HCAPLUS
CN Uridine, 2'-O-methyluridylyl-(3'→5')-5-(3-hydroxypropyl)-2'-O-methyl-, intramol. 5',5-ester, [P(S)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



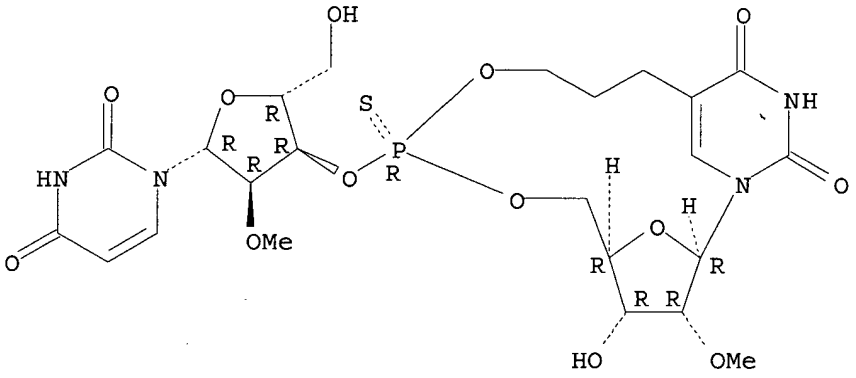
RN 305366-03-4 HCAPLUS
CN Uridine, 2'-O-methyluridylyl-(3'→5')-5-(3-hydroxypropyl)-2'-O-methyl-, intramol. 5',5-ester, [P(R)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



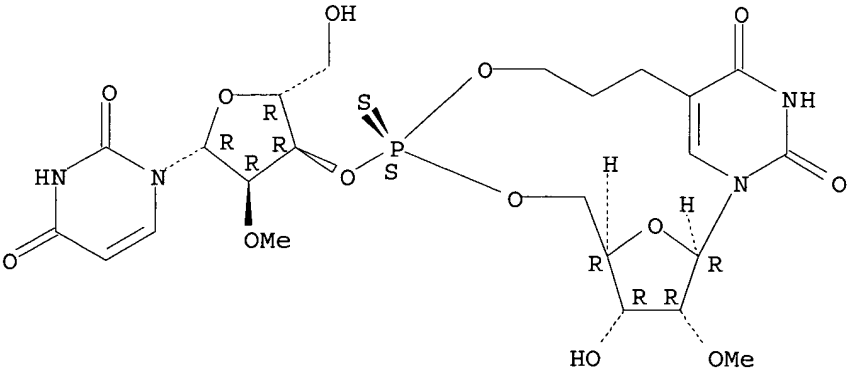
RN 305366-06-7 HCAPLUS
CN Uridine, 2'-O-methyl-P-thiouridylyl-(3'→5')-5-(3-hydroxypropyl)-2'-O-methyl-, intramol. 5',5-ester, [P(R)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 305366-07-8 HCAPLUS
CN Uridine, 2'-O-methyl-P-thiouridylyl-(3'→5')-5-(3-hydroxypropyl)-2'-O-methyl-, intramol. 5',5-ester, [P(S)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

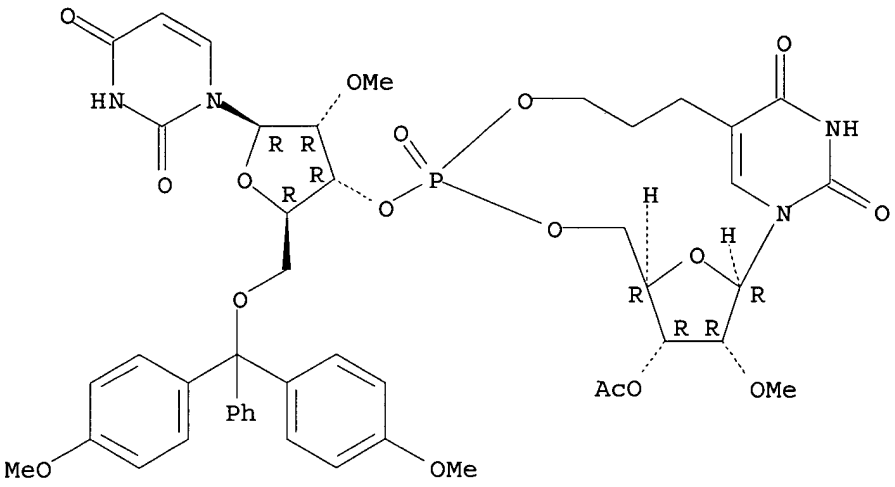


IT **305365-98-4P 305365-99-5P 305366-00-1P**
305366-01-2P 305366-04-5P 305366-05-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and properties of oligonucleotides having a phosphorus **chiral** center by incorporation of conformationally rigid 5'-cyclouridylic acid derivs.)

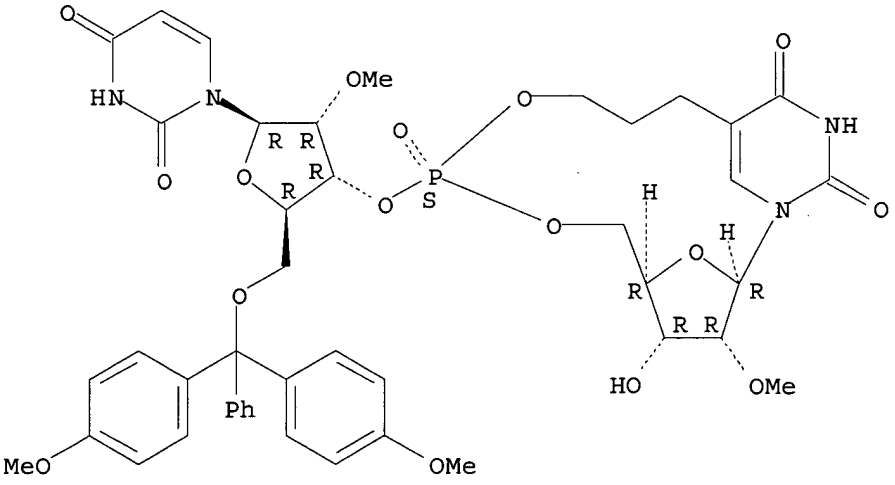
RN 305365-98-4 HCAPLUS
CN Uridine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyluridylyl-(3'→5')-5-(3-hydroxypropyl)-2'-O-methyl-, intramol. 5',5-ester, 3'-acetate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 305365-99-5 HCAPLUS
CN Uridine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyluridylyl-(3'→5')-5-(3-hydroxypropyl)-2'-O-methyl-, intramol. 5',5-ester (9CI) (CA INDEX NAME)

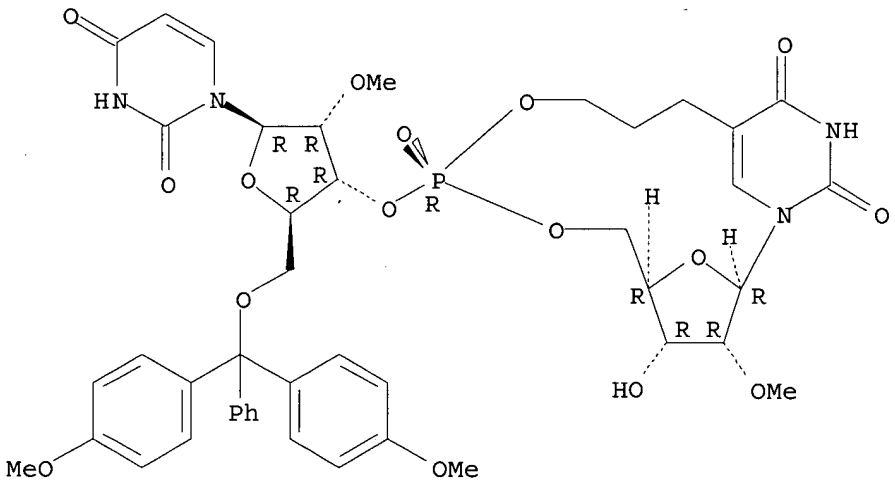
Absolute stereochemistry.



RN 305366-00-1 HCAPLUS
CN Uridine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyluridylyl-(3'→5')-5-(3-hydroxypropyl)-2'-O-methyl-, intramol. 5',5-ester,

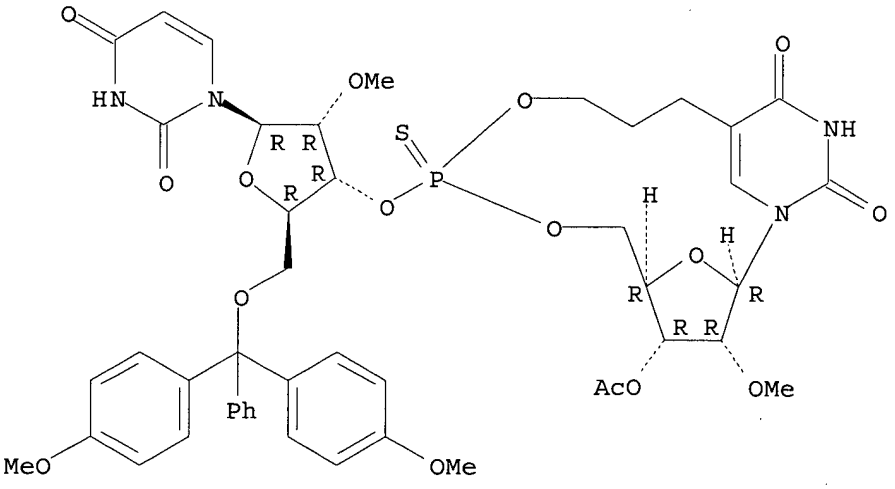
[P(R)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



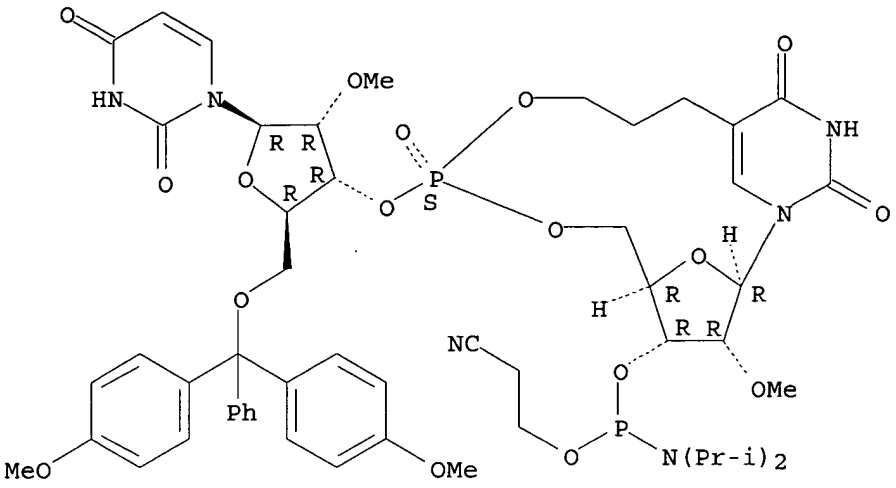
RN 305366-01-2 HCAPLUS
CN Uridine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyl-P-thiouridylyl-(3'→5')-5-(3-hydroxypropyl)-2'-O-methyl-, 3'-acetate, intramol. 5',5-ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



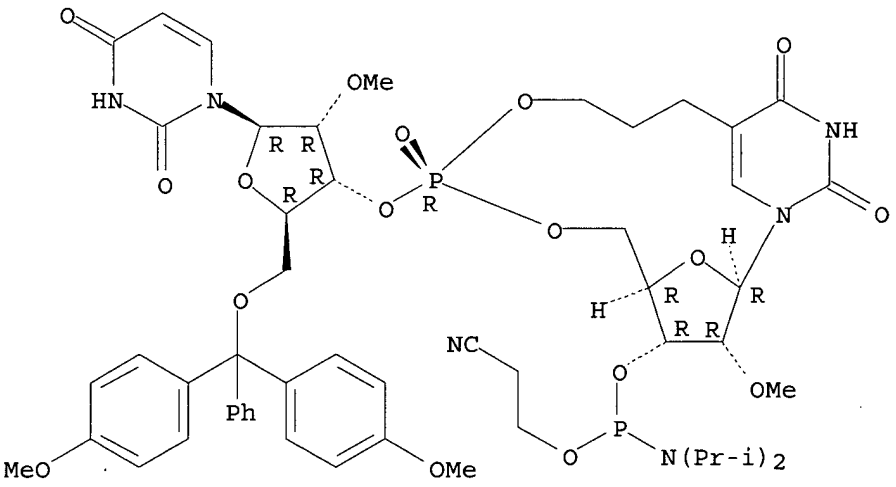
RN 305366-04-5 HCAPLUS
CN Uridine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyluridylyl-(3'→5')-5-(3-hydroxypropyl)-2'-O-methyl-, intramol. 5',5-ester, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite], [P(S)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 305366-05-6 HCAPLUS
CN Uridine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyluridylyl-(3'→5')-5-(3-hydroxypropyl)-2'-O-methyl-, intramol. 5',5-ester, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite], [P(R)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

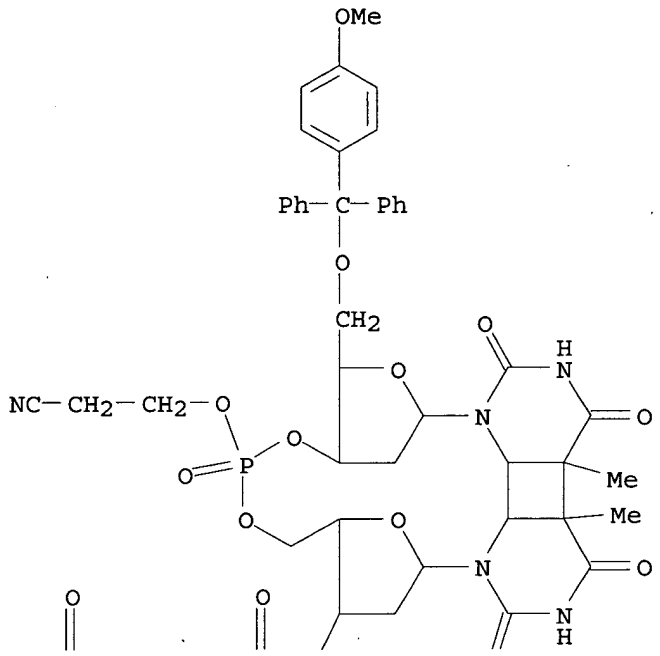


REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

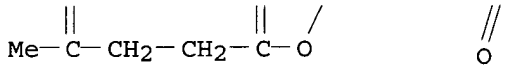
L89 ANSWER 5 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 1996:687290 HCAPLUS
DOCUMENT NUMBER: 126:3811
TITLE: Inhibition of Transcription Factor Binding by Ultraviolet-Induced Pyrimidine Dimers
AUTHOR(S): Tommasi, Stella; Swiderski, Piotr M.; Tu, Yuqing; Kaplan, Bruce E.; Pfeifer, Gerd P.
CORPORATE SOURCE: Department of Biology, Beckman Research Institute of the City of Hope, Duarte, CA, 91010, USA
SOURCE: Biochemistry (1996), 35(49), 15693-15703

CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 22 Nov 1996
AB The formation of DNA photoproducts by UV light is responsible for the induction of mutations and the development of skin cancer. Cis-syn cyclobutane pyrimidine dimers (pyrimidine dimers) are the most frequent lesions produced in DNA by UV irradiation Besides being mutagenic, pyrimidine dimers may interfere with other important DNA-dependent processes. To analyze the effects of pyrimidine dimers on the ability of DNA sequences to be recognized by trans-acting factors, we have incorporated site-specific T/\T dimers into oligonucleotides containing the recognition sequences of the sequence-specific transcription factors E2F, NF-Y, AP-1, NFκB, and p53. In each case, presence of the photodimer strongly inhibited binding of the resp. transcription factor complex. Reduction of binding varied between 11- and 60-fold. The results indicate that the most common UV-induced DNA lesion can interfere severely with binding of several important cell cycle regulatory and DNA damage responsive transcription factors. We suggest that inhibition of transcription factor binding may be a major biol. effect of UV radiation since promoter regions are known to be repaired inefficiently and since UV damage can deregulate the function of a large number of different factors.
CC 8-2 (Radiation Biochemistry)
IT Promoter (**genetic** element)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(p53 **gene**; inhibition of **transcription** factor binding by UV-induced pyrimidine dimers)
IT 133415-95-9P **183861-80-5P 183861-81-6P** 183861-82-7P **184046-81-9P 184046-82-0P 184046-83-1P 184046-84-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(inhibition of transcription factor binding by UV-induced pyrimidine dimers)
IT **183861-80-5P 183861-81-6P 184046-81-9P 184046-82-0P 184046-83-1P 184046-84-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(inhibition of transcription factor binding by UV-induced pyrimidine dimers)
RN 183861-80-5 HCAPLUS
CN Pentanoic acid, 4-oxo-, 6-(2-cyanoethoxy)hexadecahydro-3-[[(4-methoxyphenyl)diphenylmethoxy]methyl]-15a,15b-dimethyl-6-oxido-13,15,16,18-tetraoxo-9,12-epoxy-1,4-methano-1H,6H,8H-2,5,7-trioxa-12a,14,17,18a-tetraaza-6-phosphacyclohexadeca[def]biphenylen-10-yl ester (9CI) (CA INDEX NAME)

PAGE 1-A

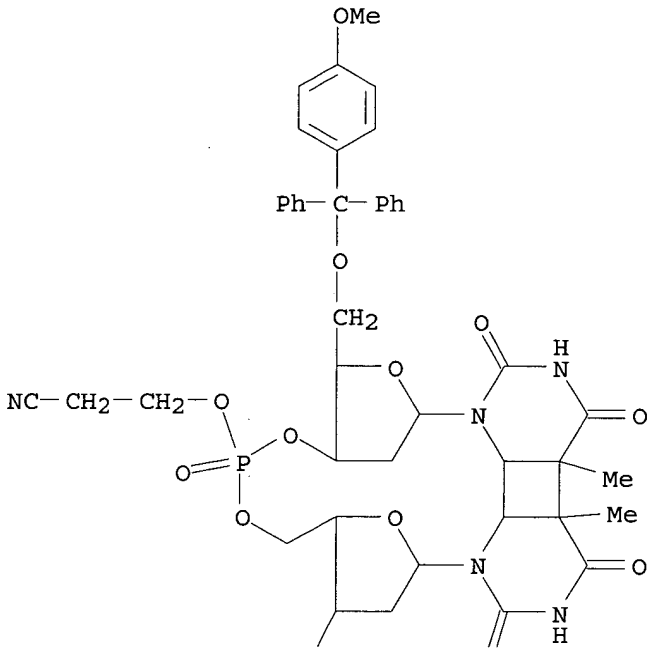


PAGE 2-A



RN 183861-81-6 HCAPLUS
CN Propanenitrile, 3-[[hexadecahydro-10-hydroxy-3-[[(4-methoxyphenyl)diphenylmethoxy]methyl]-15a,15b-dimethyl-6-oxido-13,15,16,18-tetraoxo-9,12-epoxy-1,4-methano-1H,6H,8H-2,5,7-trioxa-12a,14,17,18a-tetraaza-6-phosphacyclohexadeca[def]biphenylen-6-yl]oxy]- (9CI) (CA INDEX NAME)

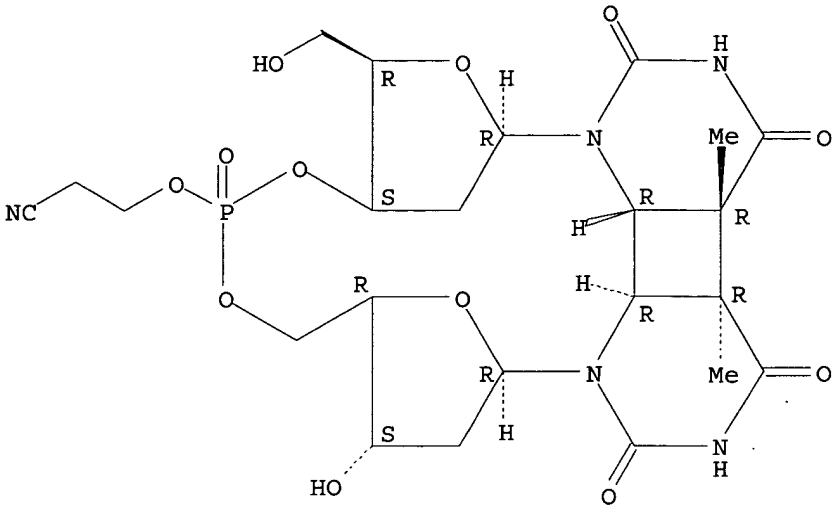
PAGE 1-A



PAGE 2-A

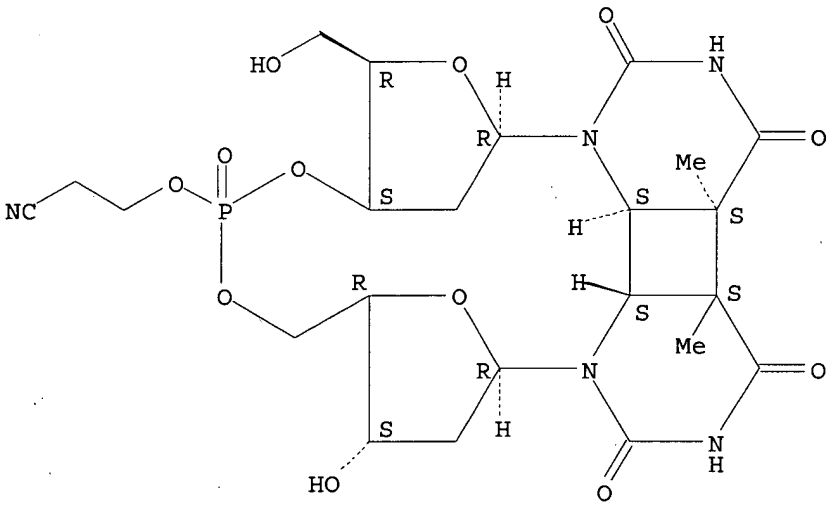
RN 184046-81-9 HCAPLUS
CN Propanenitrile, 3-[[hexadecahydro-10-hydroxy-3-(hydroxymethyl)-15a,15b-dimethyl-6-oxido-13,15,16,18-tetraoxo-9,12-epoxy-1,4-methano-1H,6H,8H-2,5,7-trioxa-12a,14,17,18a-tetraaza-6-phosphacyclohexadeca[def]biphenylen-6-yl]oxy]-, [1R-(1R*,3R*,4S*,9R*,10S*,12R*,15aR*,15bR*,18bR*,18cR*)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



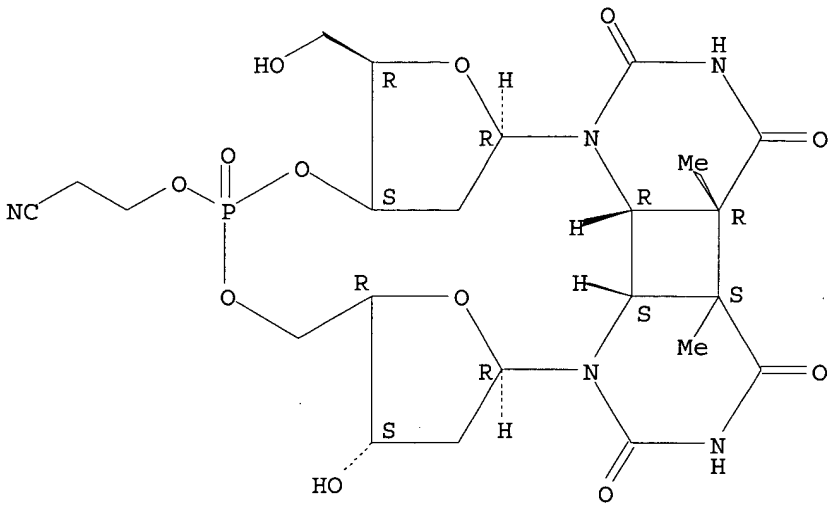
RN 184046-82-0 HCAPLUS
CN Propanenitrile, 3-[[hexadecahydro-10-hydroxy-3-(hydroxymethyl)-15a,15b-dimethyl-6-oxido-13,15,16,18-tetraoxo-9,12-epoxy-1,4-methano-1H,6H,8H-2,5,7-trioxa-12a,14,17,18a-tetraaza-6-phosphacyclohexadeca[def]biphenylen-6-yl]oxy]-, [1R-(1R*,3R*,4S*,9R*,10S*,12R*,15aS*,15bS*,18bS*,18cS*)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



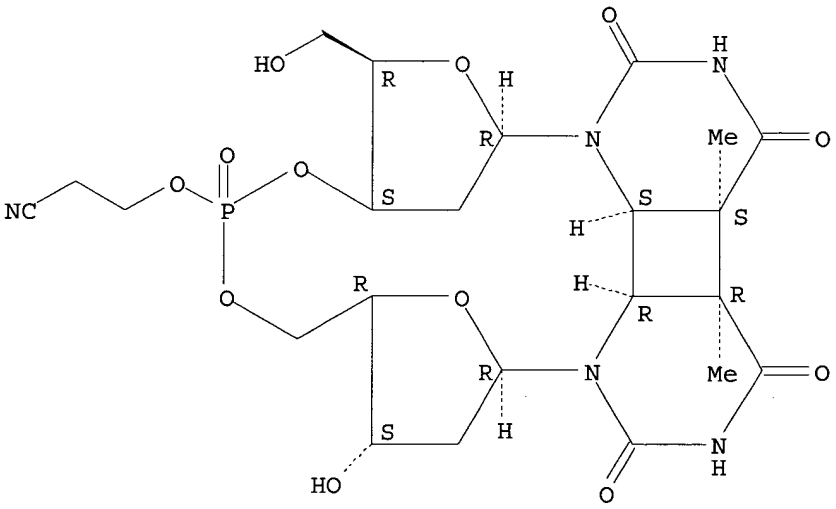
RN 184046-83-1 HCAPLUS
CN Propanenitrile, 3-[[hexadecahydro-10-hydroxy-3-(hydroxymethyl)-15a,15b-dimethyl-6-oxido-13,15,16,18-tetraoxo-9,12-epoxy-1,4-methano-1H,6H,8H-2,5,7-trioxa-12a,14,17,18a-tetraaza-6-phosphacyclohexadeca[def]biphenylen-6-yl]oxy]-, [1R-(1R*,3R*,4S*,9R*,10S*,12R*,15aS*,15bR*,18bR*,18cS*)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 184046-84-2 HCAPLUS
CN Propanenitrile, 3-[[hexadecahydro-10-hydroxy-3-(hydroxymethyl)-15a,15b-dimethyl-6-oxido-13,15,16,18-tetraoxo-9,12-epoxy-1,4-methano-1H,6H,8H-2,5,7-trioxa-12a,14,17,18a-tetraaza-6-phosphacyclohexadeca[def]biphenylen-6-yl]oxy]-, [1R-(1R*,3R*,4S*,9R*,10S*,12R*,15aR*,15bS*,18bS*,18cR*)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 6 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 1996:260542 HCAPLUS
DOCUMENT NUMBER: 124:335911
TITLE: Mutation spectra of TA*, the major photoproduct of thymidylyl-(3'-5')-deoxyadenosine, in Escherichia coli under SOS conditions
AUTHOR(S): Zhao, Xiaodong; Taylor, John-Stephen
CORPORATE SOURCE: Dep. Chemistry, Washington Univ., St. Louis, MO, 63130-4899, USA

SOURCE: Nucleic Acids Research (1996), 24(8), 1561-5
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 03 May 1996

AB The biol. activity of TA*, the major photoproduct of thymidylyl-(3',5')-deoxyadenosine, has remained speculative since it was identified a decade ago. To determine the mutagenicity of TA* in Escherichia coli, we constructed the replicative form of an M13mp18-derived phage containing TA* in the (-)-strand by polymerase-catalyzed elongation of a TA*-containing 49mer opposite a uracil-containing (+)-strand of the phage. The in vitro synthesis mixture was transfected into an ung+, phr- E. coli host and the progeny were screened with a hybridization probe unique for the (-)-strand. TA* was found to block DNA replication substantially in the absence of SOS, but under SOS, TA* was bypassed more efficiently and was highly mutagenic. Among 56 analyzed (-)-strand progeny from two transfections, 46 (82%) were mutants, including six (11%) tandem mutants. The most abundant mutation was a 3'A→T substitution (31/46, 56%). The possible biol. consequences of TA* formation in the highly conserved TATA box consensus sequence on **gene expression** are discussed in light of the mutagenicity of TA*.

CC 6-2 (General Biochemistry)
Section cross-reference(s): 3

IT **Transcription, genetic**
(mutation spectra of TA*, the major photoproduct of thymidylyl-(3'-5')-deoxyadenosine, in Escherichia coli under SOS conditions)

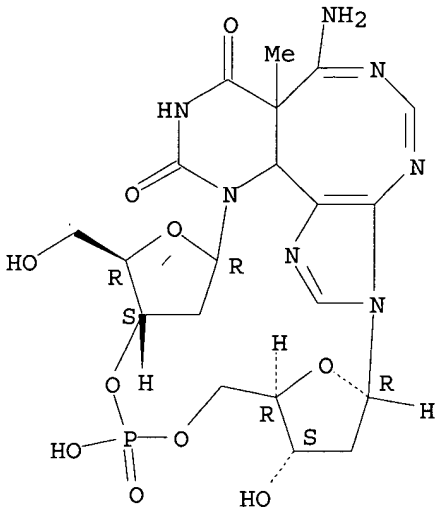
IT **176798-71-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(mutation spectra of TA*, the major photoproduct of thymidylyl-(3'-5')-deoxyadenosine, in Escherichia coli under SOS conditions)

IT **176798-71-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(mutation spectra of TA*, the major photoproduct of thymidylyl-(3'-5')-deoxyadenosine, in Escherichia coli under SOS conditions)

RN 176798-71-3 HCAPLUS

CN 3H-Imidazo[4,5-d]pyrimido[4,5-f][1,3]diazocine-8,10(9H,11H)-dione, 7-amino-3-(2-deoxy-β-D-erythro-pentofuranosyl)-11-(2-deoxy-3-O-phosphono-β-D-erythro-pentofuranosyl)-7a,11a-dihydro-7a-methyl-, intramol. 3',5''-ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 7 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 1995:973412 HCAPLUS
DOCUMENT NUMBER: 124:22726
TITLE: Binding of phosphorothioate **oligodeoxynucleotides** to basic fibroblast growth factor, recombinant soluble CD4, laminin and fibronectin is P-**chirality** independent
AUTHOR(S): Benimetskaya, Lyuba; Tonkinson, John L.; Koziolkiewicz, Maria; Karwowski, Boleslaw; Guga, Piotr; Zeltser, Ross; Stec, Wojciech; Stein, C. A.
CORPORATE SOURCE: College Physicians Surgeons, Columbia University, New York, NY, 10032, USA
SOURCE: Nucleic Acids Research (1995), 23(21), 4239-45
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 08 Dec 1995
AB Antisense **oligodeoxynucleotides** can selectively inhibit the **expression** of individual **genes** and thus have potential applications in anticancer and antiviral therapy. A critical prerequisite to their use as therapeutic agents is the understanding of their non-specific interactions with biol. structures, e.g. proteins. In this study we examined the interactions of P-**chiral** phosphorothioate **oligodeoxynucleotides** with several proteins. The Rp- and Sp-diastereomers, and racemic machine-made mixts., or M-**oligodeoxynucleotides** were used independently as competitors of the binding of a probe, phosphodiester **oligodeoxynucleotide** bearing a 5' alkylating moiety, to reCD4, bFGF and laminin. These **oligodeoxynucleotides** were also used as competitors of the binding of a non-alkylating probe M-phosphorothioate **oligodeoxynucleotide**, 5'-32P-SdT18 to fibronectin. The average values of and quant. ests. for the IC50 of competition and the constant of competition (Kc) of Rp-, Sp- and M-stereoisomers of several homo- and heteropolymer **oligodeoxynucleotides** were determined and compared. Surprisingly, in the proteins we studied, the values of IC50 and Kc for the Rp-, Sp- and M-**oligodeoxynucleotides** were essentially identical. Thus, the ability of the phosphorothioate **oligodeoxynucleotides** were

employed, to bind to the proteins studied in this work, is virtually independent of P-**chirality**. Our results also imply that the role of the purine and pyrimidine bases in **oligodeoxynucleotide** -protein interactions, as well as the nature of the contact points (sulfur vs. oxygen) between the oligomer and the protein, may be relatively unimportant.

CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 6

ST phosphorothioate **oligodeoxyribonucleotide** binding bFGF **Pchirality** independent; CD4 binding phosphorothioate **oligodeoxyribonucleotide Pchirality** independent; laminin binding phosphorothioate **oligodeoxyribonucleotide Pchirality** independent; fibronectin binding phosphorothioate **oligodeoxyribonucleotide Pchirality** independent

IT **Chirality**
(P-; binding of phosphorothioate **oligodeoxynucleotides** to basic fibroblast growth factor, recombinant soluble CD4, laminin and fibronectin is P-**chirality** independent)

IT Fibronectins
Laminins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(binding of phosphorothioate **oligodeoxynucleotides** to basic fibroblast growth factor, recombinant soluble CD4, laminin and fibronectin is P-**chirality** independent)

IT Antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(CD4, binding of phosphorothioate **oligodeoxynucleotides** to basic fibroblast growth factor, recombinant soluble CD4, laminin and fibronectin is P-**chirality** independent)

IT **Nucleotides, biological studies**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**oligo**-, **deoxyribo**-, M-; the Rp- and Sp-diastereomers, and racemic machine-made mixts., or M-oligodeoxynucleotides were used as competitors of the binding of a probe, phosphodiester oligodeoxynucleotide bearing a 5' alkylating moiety, to reCD4, bFGF and laminin)

IT **Nucleotides, biological studies**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**oligo**-, **deoxyribo**-, **thiophosphate-linked**, binding of phosphorothioate **oligodeoxynucleotides** to basic fibroblast growth factor, recombinant soluble CD4, laminin and fibronectin is P-**chirality** independent)

IT 106096-93-9, Basic fibroblast growth factor
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(binding of phosphorothioate **oligodeoxynucleotides** to basic fibroblast growth factor, recombinant soluble CD4, laminin and fibronectin is P-**chirality** independent)

L89 ANSWER 8 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 9
ACCESSION NUMBER: 1992:523838 HCAPLUS
DOCUMENT NUMBER: 117:123838
TITLE: Phosphorothioate oligodeoxynucleotides. Anti-sense inhibitors of **gene expression**?
AUTHOR(S): Stein, C. A.; Tonkinson, John L.; Yakubov, L.

CORPORATE SOURCE: Compr. Cancer Cent., Columbia Univ., New York, NY, 10032, USA
SOURCE: Pharmacology & Therapeutics (1991), 52(3), 365-84
CODEN: PHTHDT; ISSN: 0163-7258
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 04 Oct 1992
AB A review with .apprx.90 refs. Phosphorothioate (PS) **oligodeoxynucleotides** are relatively nuclease-resistant, water-soluble analogs of phosphodiester (PO) **oligodeoxynucleotides.** These mols. are **chiral** but still hybridize well to their RNA targets. While considered for use as in vivo anti-sense inhibitors of **gene expression**, their biol., especially in the anti-viral area, is dominated by non-sequence specific effects. This review discusses both the sequence and non-sequence specific biol. effects of PS oligomers, and attempts to more clearly indicate their ultimate therapeutic potential.
CC 1-0 (Pharmacology)
Section cross-reference(s): 3
ST review phosphorothioate oligodeoxynucleotide **gene expression** inhibitor
IT **Gene**, animal
RL: BIOL (Biological study)
(**expression** of, phosphorothioate oligodeoxynucleotides as antisense inhibitors of)
IT **Nucleotides, polymers**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**oligo-**, **deoxyribo-**, **thiophosphate-linked**, antisense inhibitors of **gene expression**, antiviral activity of)

L89 ANSWER 9 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:324012 HCAPLUS
DOCUMENT NUMBER: 142:369833
TITLE: Hydrolases and their encoding nucleic acids from environmental samples and uses of the hydrolases, and in particular lipases, in synthetic and industrial processes
INVENTOR(S): Bornscheuer, Uwe T.; Weiner, David Paul; Hitchman, Tim; Lyon, Jonathan; Wongsakul, Sirirung
PATENT ASSIGNEE(S): Diversa Corporation, USA
SOURCE: PCT Int. Appl., 434 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005032496	A2	20050414	WO 2004-US7095	20040308

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,

ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-453450P P 20030307
US 2003-458123P P 20030325
US 2003-513332P P 20031021

ED Entered STN: 15 Apr 2005

AB The invention provides 477 hydrolases and the **polynucleotides** encoding them isolated from environmental sources, and methods of making and using these **polynucleotides** and polypeptides. In one aspect, the invention is directed to polypeptides, e.g., enzymes, having a hydrolase activity, e.g., an esterase, acylase, lipase, phospholipase (e.g., phospholipase A, B, C and D activity, patatin activity, lipid acyl hydrolase (LAH) activity) or protease activity, including thermostable and thermotolerant hydrolase activity. The hydrolase activities of the polypeptides and peptides of the invention include esterase activity, lipase activity (hydrolysis of lipids), acidolysis reactions (to replace an esterified fatty acid with a free fatty acid), transesterification reactions (exchange of fatty acids between triglycerides), ester synthesis, ester interchange reactions, phospholipase activity, and protease activity (hydrolysis of peptide bonds). The polypeptides of the invention can be used in a variety of pharmaceutical, agricultural, and industrial contexts, including the manufacture of cosmetics and nutraceuticals. In another aspect, the polypeptides of the invention are used to synthesize enantiomerically pure **chiral** products.

IC ICM A61K

CC 7-2 (Enzymes)
Section cross-reference(s): 3, 9, 17, 22, 63

IT Promoter (**genetic** element)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(35S, plant **expression** vector containing; hydrolases and their encoding nucleic acids from environmental samples and uses of the hydrolases, and in particular lipases, in synthetic and industrial processes)

IT Fusion proteins (chimeric proteins)
Promoter (**genetic** element)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(plant **expression** vector containing; hydrolases and their encoding nucleic acids from environmental samples and uses of the hydrolases, and in particular lipases, in synthetic and industrial processes)

IT **Genetic** element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(signal sequence, plant **expression** vector containing; hydrolases and their encoding nucleic acids from environmental samples and uses of the hydrolases, and in particular lipases, in synthetic and industrial processes)

IT **Antisense oligonucleotides**
Double stranded RNA
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(translation inhibition by; hydrolases and their encoding nucleic acids from environmental samples and uses of the hydrolases, and in particular lipases, in synthetic and industrial processes)

L89 ANSWER 10 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:232427 HCAPLUS

DOCUMENT NUMBER: 142:310864
TITLE: Gapped antisense **oligonucleotides** having site specific **chiral** phosphorothioate **internucleoside** linkages
INVENTOR(S): Sanghvi, Yogesh S.; Manoharan, Muthiah
PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA
SOURCE: U.S., 49 pp., Cont.-in-part of U.S. 6,440,943.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6867294	B1	20050315	US 1999-438989	19991112
US 6242589	B1	20010605	US 1998-115027	19980714
US 6440943	B1	20020827	US 1999-352058	19990714
WO 2001040515	A1	20010607	WO 2000-US30971	20001110

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 1998-115027 A1 19980714
US 1999-352058 A2 19990714
US 1999-438989 A2 19991112

ED Entered STN: 17 Mar 2005
AB Novel **chiral** compds. that mimic and/or modulate the activity of wild-type nucleic acids are disclosed. In general, the compds. are phosphorothioate **oligonucleotides** wherein the 5' and the 3'-terminal **internucleoside** linkages are **chirally** Sp and internal **internucleoside** linkages are **chirally** Rp. Thus, such **oligonucleotides** inhibiting H-ras and ICAM-1 **gene expression** were prepared and their effects demonstrated in mammalian cell culture.
IC ICM C07H021-04
ICS C07H021-00
INCL 536024500; 536024300; 536024310; 536024320; 536024330; 536025300; 536025310; 536026310; 536022100
CC 3-1 (Biochemical Genetics)
ST antisense **oligonucleotide chiral** phosphorothioate linked termini Hras ICAM1
IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD54, **gene** for, inhibition of **expression** of; gapped antisense **oligonucleotides** having site specific **chiral** phosphorothioate **internucleoside** linkages)
IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ICAM-1 (intercellular adhesion mol. 1), **gene** for, inhibition of **expression** of; gapped antisense **oligonucleotides** having site specific **chiral** phosphorothioate **internucleoside** linkages)
IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(c-Ha-ras, inhibition of expression of; gapped antisense **oligonucleotides** having site specific **chiral** phosphorothioate **internucleoside** linkages)

IT **Antisense oligonucleotides**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**chiral** phosphorothioate-linked; gapped antisense **oligonucleotides** having site specific **chiral** phosphorothioate **internucleoside** linkages)

IT 848020-79-1 848020-80-4 848020-81-5 848020-82-6 848020-83-7 848020-84-8
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(gapped antisense **oligonucleotides** having site specific **chiral** phosphorothioate **internucleoside** linkages)

REFERENCE COUNT: 312 THERE ARE 312 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 11 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:60697 HCAPLUS
DOCUMENT NUMBER: 140:141703
TITLE: Identification, cloning and sequences of microbial monooxygenases and their use for chiral synthesis and drug screening
INVENTOR(S): Richardson, Toby
PATENT ASSIGNEE(S): Diversa Corporation, USA
SOURCE: PCT Int. Appl., 199 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007750	A2	20040122	WO 2003-US22013	20030711

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-395220P P 20020711
OTHER SOURCE(S): MARPAT 140:141703
ED Entered STN: 26 Jan 2004
AB The invention provides polypeptides having a monooxygenase activity, **polynucleotides** encoding these enzymes, the use of such **polynucleotides** and polypeptides. The **nucleotide** sequences and the encoded amino acid sequences of 5 monooxygenases from environmental samples and from Streptomyces diversa are disclosed. In one aspect, the invention provides polypeptides having a monooxygenase activity, such as a Baeyer-Villiger monooxygenases, and/or enzymes for catalysis of sulfoxidn. reactions. Enzymes of the invention can have a monooxygenase, an esterases and/or a dehydrogenase activity. The monooxygenases of the invention can be used for production of **chiral**

synthetic intermediates and for drug screening.
IC ICM C12Q
CC 7-5 (Enzymes)
Section cross-reference(s): 1, 3, 9, 10, 16, 63
IT **Antisense oligonucleotides**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(identification, cloning and sequences of microbial monooxygenases and their use for **chiral** synthesis and drug screening)
IT **Translation, genetic**
(inhibition, by antisense **oligonucleotides**; identification, cloning and sequences of microbial monooxygenases and their use for **chiral** synthesis and drug screening)
IT 649785-30-8 649785-31-9 649785-32-0 649785-33-1 649785-34-2
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**nucleotide** sequence; identification, cloning and sequences of microbial monooxygenases and their use for **chiral** synthesis and drug screening)

L89 ANSWER 12 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:491367 HCAPLUS
DOCUMENT NUMBER: 139:65422
TITLE: Screening, selection, identification and sequences of cytochrome P 450 for use in the production of chiral epoxides
INVENTOR(S): Weiner, David; Burke, Mark; Hitchman, Tim; Pujol, Catherine; Richardson, Toby; Short, Jay
PATENT ASSIGNEE(S): Diversa Corporation, USA
SOURCE: PCT Int. Appl., 365 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003052050	A2	20030626	WO 2002-US24910	20020805
WO 2003052050	A3	20040513		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2456210	AA	20030626	CA 2002-2456210	20020805
US 2003180742	A1	20030925	US 2002-214446	20020805
EP 1513860	A2	20050316	EP 2002-802918	20020805
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005512532	T2	20050512	JP 2003-552917	20020805

PRIORITY APPLN. INFO.: US 2001-309497P P 20010803
WO 2002-US24910 W 20020805

ED Entered STN: 27 Jun 2003

AB The invention is directed to polypeptides having P 450 activity, **polynucleotides** encoding the polypeptides, antibodies that bind to these polypeptides, and methods for making and using these **polynucleotides** and polypeptides. The present invention relates to to methods of selecting or screening and identification of P 450 enzymes for use in the production of **chiral** epoxides. The **nucleotide** sequences and the encoded amino acid sequences of 28 P 450 enzymes of bacterial or unknown origin from environmental sources are disclosed. The P 450 enzymes can be used to catalyze the hydrolysis of epoxides and arene oxides to their corresponding diols.

IC ICM C12N

CC 7-5 (Enzymes)
Section cross-reference(s): 3, 10, 16

IT **Translation, genetic**
(inhibition, by antisense **oligonucleotides**; screening, selection, identification, cloning and sequences of cytochrome P 450 for use in production of **chiral** epoxides)

IT **Antisense oligonucleotides**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(screening, selection, identification, cloning and sequences of cytochrome P 450 for use in production of **chiral** epoxides)

IT 549679-50-7D, subfragments are claimed 549679-51-8D, subfragments are claimed 549679-52-9D, subfragments are claimed 549679-53-0D, subfragments are claimed 549679-54-1D, subfragments are claimed 549679-55-2D, subfragments are claimed 549679-56-3D, subfragments are claimed 549679-57-4D, subfragments are claimed 549679-58-5D, subfragments are claimed 549679-59-6D, subfragments are claimed 549679-60-9D, subfragments are claimed 549679-61-0D, subfragments are claimed 549679-62-1D, subfragments are claimed 549679-63-2D, subfragments are claimed 549679-64-3D, subfragments are claimed 549679-65-4D, subfragments are claimed 549679-66-5D, subfragments are claimed 549679-67-6D, subfragments are claimed 549679-68-7D, subfragments are claimed 549679-69-8D, subfragments are claimed 549679-70-1D, subfragments are claimed 549679-71-2D, subfragments are claimed 549679-72-3D, subfragments are claimed 549679-73-4D, subfragments are claimed 549679-74-5D, subfragments are claimed 549679-75-6D, subfragments are claimed 549679-76-7D, subfragments are claimed 549679-77-8D, subfragments are claimed
RL: ANT (Analyte); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**nucleotide** sequence; screening, selection, identification, cloning and sequences of cytochrome P 450 for use in production of **chiral** epoxides)

L89 ANSWER 13 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:136067 HCAPLUS
DOCUMENT NUMBER: 136:179042
TITLE: Poly(ether-thioether)-, poly(ether-sulfoxide)-, and poly(ether-sulfone) nucleic acids, their synthesis and use in medicine and biochemistry
INVENTOR(S): Segev, David
PATENT ASSIGNEE(S): Bio-Rad Laboratories, Inc., USA
SOURCE: U.S., 46 pp., Cont.-in-part of U.S. Ser. 384,995, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6348583	B1	20020219	US 1999-411862	19991004
CA 2382631	AA	20010308	CA 2000-2382631	20000721
WO 2001016365	A1	20010308	WO 2000-IL432	20000721
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1208234	A1	20020529	EP 2000-946256	20000721
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003508062	T2	20030304	JP 2001-520910	20000721
AU 769619	B2	20040129	AU 2000-60126	20000721
PRIORITY APPLN. INFO.:			US 1999-384995	B2 19990830
			US 1999-411862	A 19991004
			WO 2000-IL432	W 20000721

ED Entered STN: 21 Feb 2002

AB A compound comprising a poly(ether-thioether), poly(ether-sulfoxide) or poly(ether-sulfone) backbone bearing a plurality of ligands that are individually bound to **chiral** carbon atoms located within the backbone, at least one of the ligands including a moiety such as a naturally occurring **nucleobase**, a **nucleobase** binding group; a process of synthesizing the compound; monomers to be used in this process and their synthesis; and processes for using the compound in biochem. (e.g., in hybridization) and medicine (e.g., as pharmaceuticals to treat diseases or viral infections) are disclosed.

IC ICM C07H019-00
ICS C07H021-00; C07H021-02; C07H021-04; A01N061-00

INCL 536023100

CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 1, 6, 33, 35

IT **Gene**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (**expression**, inhibition of; poly(ether-thioether)-, poly(ether-sulfoxide)-, and poly(ether-sulfone) nucleic acids, their synthesis and use in medicine and biochem.)

IT **2476-57-5** 399597-12-7 399597-13-8 399597-14-9 399597-15-0 399597-16-1
RL: PRP (Properties)
(unclaimed sequence; poly(ether-thioether)-, poly(ether-sulfoxide)-, and poly(ether-sulfone) nucleic acids, their synthesis and use in medicine and biochem.)

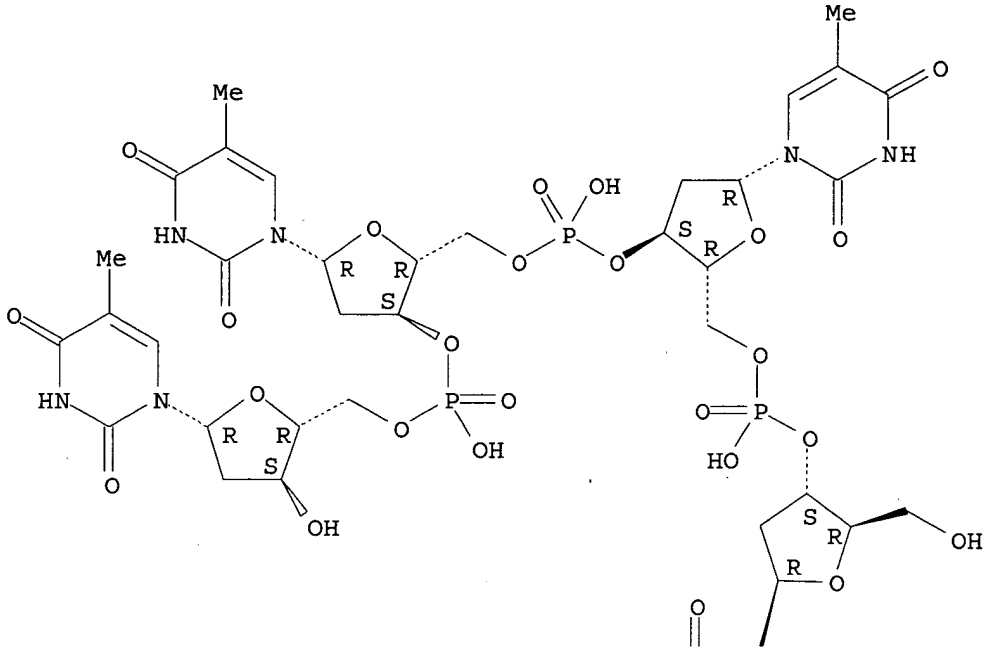
IT **2476-57-5**
RL: PRP (Properties)
(unclaimed sequence; poly(ether-thioether)-, poly(ether-sulfoxide)-, and poly(ether-sulfone) nucleic acids, their synthesis and use in medicine and biochem.)

RN 2476-57-5 HCAPLUS

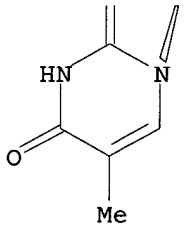
CN Thymidine, thymidylyl-(3'→5')-thymidylyl-(3'→5')-thymidylyl-(3'→5')- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 14 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:815867 HCAPLUS
DOCUMENT NUMBER: 136:128433
TITLE: Targeting of cancer-related proteins with PNA oligomers
AUTHOR(S): Pooga, Margus; Langel, Ulo
CORPORATE SOURCE: Estonian Biocentre, Tartu, EE-51010, Estonia
SOURCE: Current Cancer Drug Targets (2001), 1(3), 231-239
CODEN: CCDTB9; ISSN: 1568-0096
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 09 Nov 2001
AB A review. Aberrant **gene expression** is characteristic to all cancer cells and pathophysiol. in general. Selective inhibition of

constitutively elevated **expression** of **oncogenes** provides an opportunity to hinder the proliferation of malignant cells. Small synthetic mols. that specifically interfere with transcription and/or translation have great potential as anticancer drugs. Currently first-generation antisense **oligonucleotides** are widely used to inhibit the **oncogene expression.** The second generation of antisense agents have been studied mainly in vitro. One of these agents, peptide nucleic acid (PNA) is an **oligonucleotide** mimic with a noncharged **achiral** polyamide backbone to which the **nucleobases** are linked. PNA oligomers bind tightly to complementary DNA or RNA and are very stable in biol. fluids. PNA can inhibit **transcription** and **translation** of target **genes** by specifically hybridizing to DNA or mRNA. The in vitro expts. showing inhibition of target protein expression by PNA have been followed by the first successful applications of PNA as an antisense agent in cultured cells and also in vivo. Hopefully this will lead to a wider use of PNA in the studies of cancer biol. and therapy.

CC 1-0 (Pharmacology)

ST review antisense oligonucleotide peptide nucleic acid antitumor **oncogene expression**

IT **Gene**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**expression**, **oncogene**; targeting of cancer-related proteins with PNA oligomers)

IT **Gene**, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**oncogene**, **expression**; targeting of cancer-related proteins with PNA oligomers)

IT Antitumor agents
Transcription, genetic
Translation, genetic
(targeting of cancer-related proteins with PNA oligomers)

IT **Antisense oligonucleotides**
Peptide nucleic acids
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeting of cancer-related proteins with PNA oligomers)

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 15 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:475786 HCAPLUS
DOCUMENT NUMBER: 133:99558
TITLE: Modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and the therapeutic uses thereof
INVENTOR(S): Dale, Roderic M. K.; Arrow, Amy; Thompson, Terry
PATENT ASSIGNEE(S): Oligos Etc. Inc., USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040714	A2	20000713	WO 1999-US29976	19991215
WO 2000040714	A3	20001102		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,

CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2357950	AA	20000713	CA 1999-2357950	19991215
EP 1141278	A2	20011010	EP 1999-968130	19991215
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002534086	T2	20021015	JP 2000-592411	19991215
US 2003045490	A1	20030306	US 2002-76597	20020219
PRIORITY APPLN. INFO.:			US 1998-223586 A	19981230
			US 1999-364626 A	19990729
			WO 1999-US29976 W	19991215

ED Entered STN: 14 Jul 2000

AB The invention provides end-blocked acid resistant antisense oligonucleotides targeted at inhibiting **expression** of **genes** coding for Phosphodiesterase 4 (PDE4). The oligonucleotides of this invention exhibit substantial stability at low pH, substantial resistance to nuclease degradation, low toxicity and binding specificity both in vivo and in vitro. The invention further relates to the therapeutic uses of oligonucleotides of this invention in treatment of PDE4-mediated diseases.

IC ICM C12N015-11
ICS C07H021-02; A61K031-712; A61P017-00; A61P029-00

CC 1-7 (Pharmacology)
Section cross-reference(s): 3, 7, 63

ST antisense oligonucleotide phosphodiesterase 4 **gene expression** therapy

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(2'-O-alkyl end-blocked; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(2'-O-alkyl-n(O-alkyl) end-blocked; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Gene**, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PDE4, inhibition of **expression** of; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT Nose
(allergic rhinitis, modified antisense oligonucleotide effects on; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT Dermatitis
(atopic, B cell or T cell-mediated; chemical-induced, effects of modified antisense oligonucleotides on; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological

study); PREP (Preparation); USES (Uses)
(backbone structure includes 2'-O-Me linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes 2'-O-alkyl nucleotides; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes 2'-O-alkyl-n(O-alkyl) phosphodiesters; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes 2'-deoxy-erythropentofuranosyl; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes 2'-fluoro; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes 2'-halogens; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes 3'-3' linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes 3'-O-alkyl-n-(O-alkyl); modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes 3'-O-alkyl; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes 3'-halogens; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological

study); PREP (Preparation); USES (Uses)
(backbone structure includes 5'-2' linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes 5'-5' linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes PNA linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes acetamidate linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes aminoalkylphosphorothioamidate linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes bridged methylene phosphonate linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes bridged phosphoramidate linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes bridged phosphorodithioate linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes carbamate linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes carbonate linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological

study); PREP (Preparation); USES (Uses)
(backbone structure includes carboxymethylester linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes **chiral** phosphorous linkages; modified antisense **oligonucleotides** for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes formacetal/ketal linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes four residue group linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes methylphosphonate linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
Antisense oligonucleotides
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes morpholino linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes phosphodiester linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes phosphoramidate linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes phosphoramidates; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes phosphorodithioate linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes phosphorothioate linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes phosphotriester linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes siloxane linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes sulfamate linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes sulfamide linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes sulfide linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes sulfone internucleotide linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes sulfoxide linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes thioether linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(backbone structure includes thioformacetal linkages; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT mRNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(encoding PDE4, antisense oligonucleotides hybridizes to; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT Anti-inflammatory agents
DNA sequences
(modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT Drug delivery systems
(nasal, for PDE4 antisense oligonucleotides; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(p-ethoxy; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(p-iso-Pr; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT **Antisense oligonucleotides**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protonated; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT Drug delivery systems
(topical, for PDE4 antisense oligonucleotides; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT Skin, disease
(wheal-flare reaction, modified antisense oligonucleotide effects on; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT 9036-21-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IV; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT 282121-11-3P 283616-55-7P 283616-56-8P 283616-57-9P 283616-58-0P
283616-59-1P 283616-60-4P 283616-61-5P 283616-62-6P 283616-63-7P
283616-64-8P 283616-65-9P 283616-66-0P 283616-67-1P 283616-68-2P
283616-69-3P 283616-70-6P 283616-71-7P 283616-72-8P 283616-73-9P
283616-74-0P 283616-75-1P 283616-76-2P 283616-77-3P 283616-78-4P
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283616-84-2P 283616-85-3P 283616-86-4P 283616-87-5P 283616-88-6P
283616-89-7P 283616-90-0P 283616-91-1P 283616-92-2P 283616-93-3P
283616-94-4P 283616-95-5P 283616-96-6P 283616-97-7P 283616-98-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and therapeutic uses thereof)

IT 148067-93-0 151912-83-3 165725-18-8 176521-94-1 202077-52-9

213322-69-1
RL: PRP (Properties)
(unclaimed protein sequence; modified antisense oligonucleotides for inhibiting phosphodiesterase 4 **gene expression** and the therapeutic uses thereof)

L89 ANSWER 16 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:475686 HCAPLUS
DOCUMENT NUMBER: 133:105347
TITLE: Cyclic polyamides which bind sequence-specifically to DNA and their use for control of **gene expression**
INVENTOR(S): Baird, Eldon E.; Dervan, Peter B.
PATENT ASSIGNEE(S): Genesoft, Inc., USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040605	A2	20000713	WO 2000-US298	20000106
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2358119	AA	20000713	CA 2000-2358119	20000106
EP 1144414	A2	20011017	EP 2000-903143	20000106
EP 1144414	B1	20041006		
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JP 2002539077	T2	20021119	JP 2000-592313	20000106
US 6673940	B1	20040106	US 2000-479279	20000106
AT 278693	E	20041015	AT 2000-903143	20000106
PRIORITY APPLN. INFO.:			US 1999-115232P P	19990108
			WO 2000-US298 W	20000106

ED Entered STN: 14 Jul 2000
AB The design, synthesis, and use of cyclic compds., including cyclic polyamides, is described. Such compds. comprise at least two polymer portions, one of which comprises at least three mol. units, and the other comprises at least four mol. units. At least one mol. unit of such a compound is a hydrogen bond donor or acceptor. The polymer portions are covalently linked to form a cycle. These compds. are capable of targeting specific **nucleotide** sequences in double-stranded nucleic acids, particularly double-stranded DNA. Accordingly, such compds. can be used to modulate, e.g., increase or decrease, the **expression** of one or more **genes** in vitro or in vivo. Thus, two **chiral** cyclic polyamides, cyclo-(γ-Im-Py-Py-Py-(R)H,Nγ-Im-Py-Py-Py-) and cyclo-(γ-Im-Py-Py-Py-(R)H,Nγ-Py-Py-Py-Py-) (Im = N-methylimidazole, Py = N-methylpyrrole, γ = 4-aminobutyric acid, (R)γ = (R)-2,4-diaminobutyric acid) were synthesized and shown to bind specifically to 5'-AGTACT-3' and 5'-AGTATT-3', resp. The former polyamide was found to bind to 5'-AGTACT-3' with an equilibrium associate constant

of Ka = 1.3 X 109 M-1 and with a 55-fold specificity over the single base pair mismatch sequence 5'-AGTATT-3'. This represents an 8-fold increase relative to the control "hairpin" polyamide (i.e., non-cyclic analog).

IC ICM C07K014-00

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

ST polyamide cyclic **gene expression**; pathogen infection
treatment cyclic polyamide

IT Polyamides, preparation
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclic; cyclic polyamides which bind sequence-specifically to DNA and their use for control of **gene expression**)

IT **Gene**
(**expression**; cyclic polyamides which bind sequence-specifically to DNA and their use for control of **gene expression**)

IT Pathogen
(infections, treatment of; cyclic polyamides which bind sequence-specifically to DNA and their use for control of **gene expression**)

IT **282088-63-5**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cyclic polyamides which bind sequence-specifically to DNA and their use for control of **gene expression**)

IT 222417-58-5P 222417-60-9P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclic polyamides which bind sequence-specifically to DNA and their use for control of **gene expression**)

IT **191916-06-0**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(double-stranded; cyclic polyamides which bind sequence-specifically to DNA and their use for control of **gene expression**)

IT 282739-50-8, 36: PN: US6087478 FIG: 5 unclaimed DNA 282739-51-9, 37: PN: US6087478 FIG: 5 unclaimed DNA 282739-52-0, 38: PN: US6087478 FIG: 5 unclaimed DNA 282739-53-1, 39: PN: US6087478 FIG: 5 unclaimed DNA
RL: PRP (Properties)
(unclaimed nucleotide sequence; cyclic polyamides which bind sequence-specifically to DNA and their use for control of **gene expression**)

IT **282088-63-5**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cyclic polyamides which bind sequence-specifically to DNA and their use for control of **gene expression**)

RN 282088-63-5 HCAPLUS

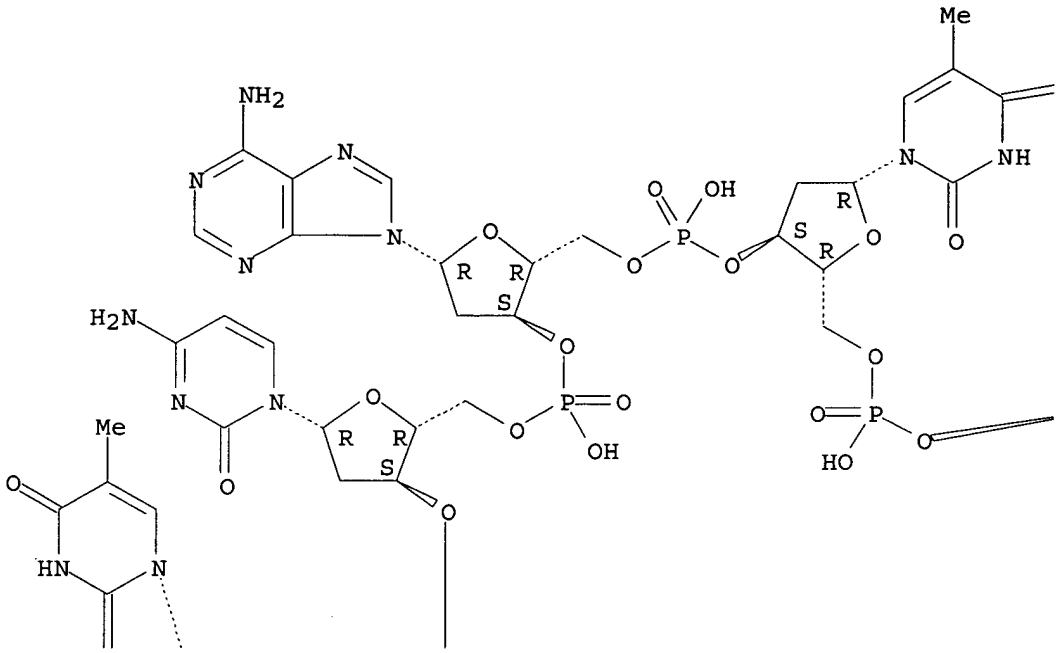
CN Thymidine, 2'-deoxyadenylyl-(3'→5')-2'-deoxyadenylyl-(3'→5')-thymidylyl-(3'→5')-2'-deoxyadenylyl-(3'→5')-2'-deoxycytidylyl-(3'→5')-, double-stranded complementary (9CI) (CA INDEX NAME)

CM 1

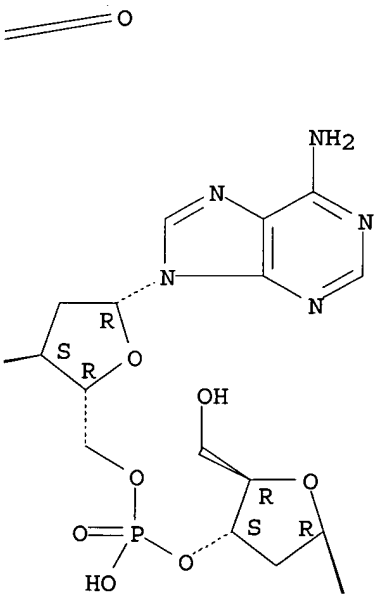
CRN 282088-62-4
CMF C59 H75 N22 O33 P5

Absolute stereochemistry.

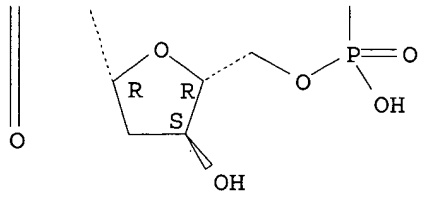
PAGE 1-A



PAGE 1-B



PAGE 2-A



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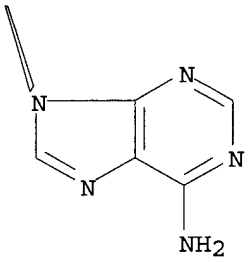
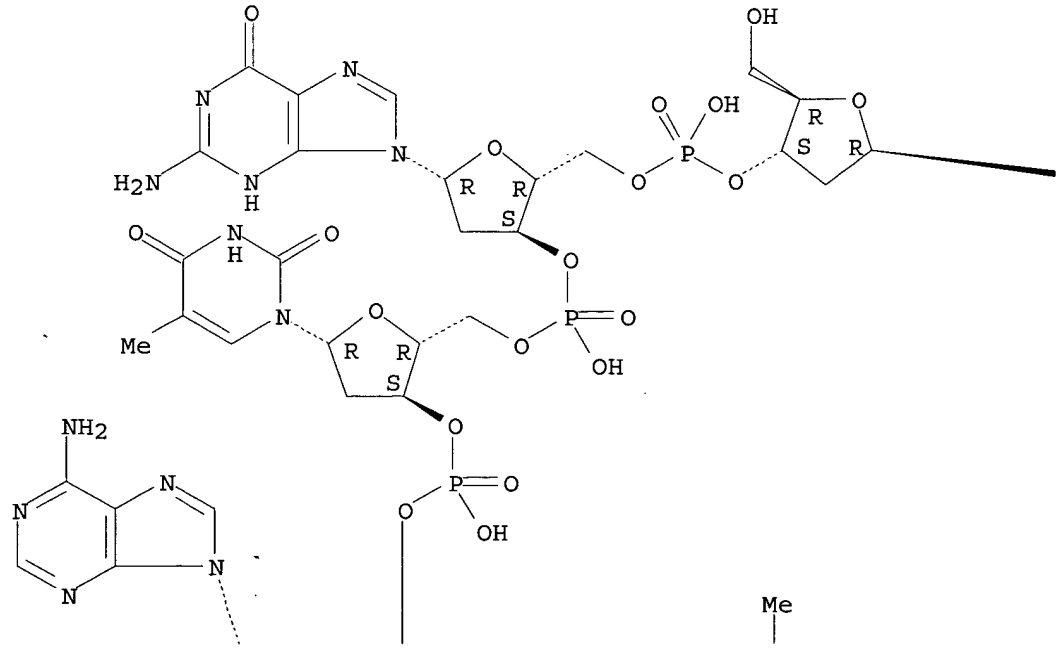


CM 2

CRN 191916-07-1
CMF C60 H76 N21 O35 P5

Absolute stereochemistry.

PAGE 1-A



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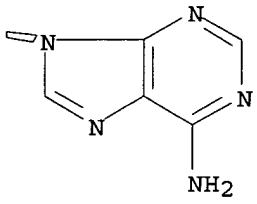
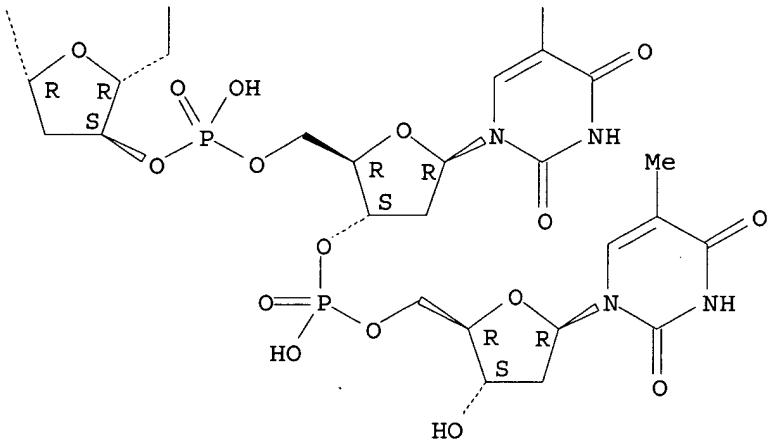


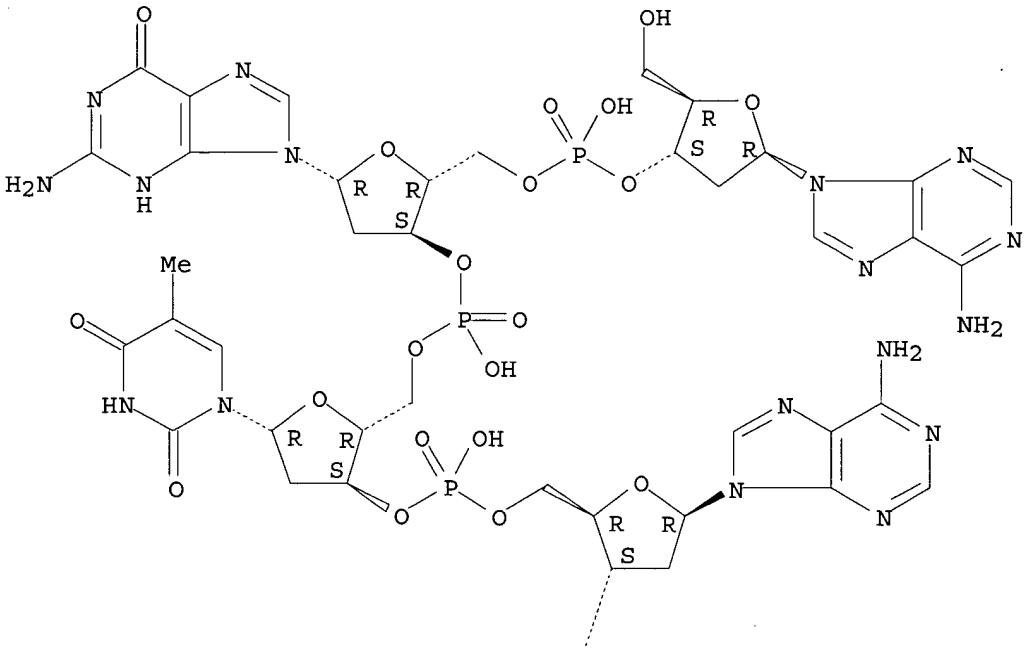
PAGE 2-A



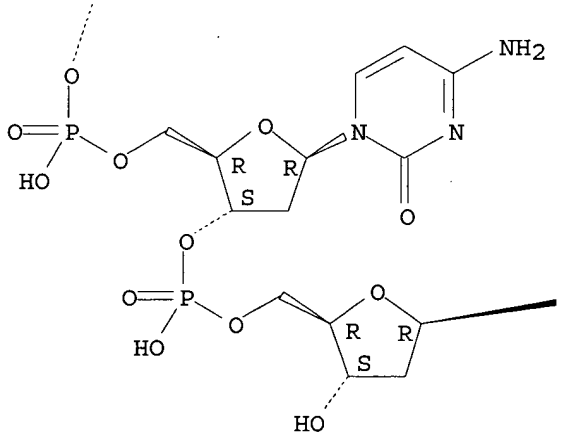
IT **191916-06-0**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(double-stranded; cyclic polyamides which bind sequence-specifically to DNA and their use for control of **gene expression**)
RN 191916-06-0 HCAPLUS
CN Thymidine, 2'-deoxyadenylyl-(3'→5')-2'-deoxyguanylyl-(3'→5')-thymidylyl-(3'→5')-2'-deoxyadenylyl-(3'→5')-2'-deoxycytidylyl-(3'→5')- (9CI) (CA INDEX NAME)

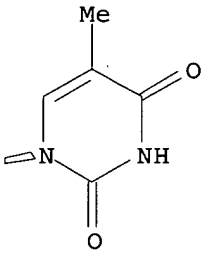
Absolute stereochemistry.

PAGE 1-A



PAGE 2-A





L89 ANSWER 17 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:68469 HCAPLUS
DOCUMENT NUMBER: 132:119023
TITLE: **Chiral** phosphorothioate-linked **oligonucleotides** and their synthesis and use in diagnosis and therapy
INVENTOR(S): Cook, Phillip Dan; Manoharan, Muthiah
PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000004034	A2	20000127	WO 1999-US15960	19990714
WO 2000004034	A3	20000622		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6242589	B1	20010605	US 1998-115027	19980714
AU 9951022	A1	20000207	AU 1999-51022	19990714
EP 1097162	A2	20010509	EP 1999-935570	19990714
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002520420	T2	20020709	JP 2000-560140	19990714
US 2001027251	A1	20011004	US 2001-805630	20010314
US 6811975	B2	20041102		
PRIORITY APPLN. INFO.:			US 1998-115027 A2	19980714
			WO 1999-US15960 W	19990714

ED Entered STN: 28 Jan 2000
AB Novel **chiral** compds. that mimic and/or modulate the activity of wild-type nucleic acids are disclosed. In general, the compds. are

phosphorothioate **oligonucleotides** wherein the 5', and the 3'-terminal **internucleoside** linkages are **chirally** Sp and internal **internucleoside** linkages are different, i.e., 5'-T1-(Nu-Sp)n-(Nu-Lp)m-(Nu-Sp)p-Nu-T2-3' (T1,T2=OH, covalent attachment to a support, etc.; Sp=Sp phosphorothioate **internucleoside** linkage; Lp=Rp phosphorothioate-, racemic phosphorothioate-, other **internucleotide** linkage; n,m=1-100; p=0-100; Nu=ribo- or **deoxyribonucleoside** and derivs.). A method for synthesizing these **oligonucleotides** comprises reaction of I [B=heterocyclic base, R1=H, (protected) OH, (protected) 2'-substituent; R2=II, III, IV; R3=protecting group] with an immobilized **nucleoside** followed by reaction of the resulting (deprotected) **dinucleotide** with I in which the II, III, IV groups have the opposite (Rp) stereochem., etc.

IC ICM C07H

CC 6-2 (General Biochemistry)
Section cross-reference(s): 1, 3, 9, 33

ST **oligonucleotide chiral** phosphorothioate linkage diagnosis therapy; synthesis phosphorothioate linked **oligonucleotide chiral** synthon

IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ICAM-1 (intercellular adhesion mol. 1), regulation of cellular production of; **chiral** phosphorothioate-linked **oligonucleotides** and their synthesis and use in diagnosis and therapy)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(c-Ha-ras, regulation of expression of; **chiral** phosphorothioate-linked **oligonucleotides** and their synthesis and use in diagnosis and therapy)

IT **Gene**, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(c-raf, regulation of **expression** of; **chiral** phosphorothioate-linked **oligonucleotides** and their synthesis and use in diagnosis and therapy)

IT **Oligonucleotides**
RL: ARG (Analytical reagent use); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**chiral** phosphorothioate-linked **oligonucleotides** and their synthesis and use in diagnosis and therapy)

IT Hepatitis C virus
(inhibition of pathogenicity of; **chiral** phosphorothioate-linked **oligonucleotides** and their synthesis and use in diagnosis and therapy)

IT 255815-60-2P 255815-61-3P
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(**chiral** phosphorothioate-linked **oligonucleotides** and their synthesis and use in diagnosis and therapy)

IT 66221-60-1 79563-59-0 125251-02-7 255391-65-2 255391-68-5 255391-71-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(**chiral** phosphorothioate-linked **oligonucleotides** and their synthesis and use in diagnosis and therapy)

IT **255391-66-3P 255391-67-4P 255391-69-6P 255391-70-9P 255391-72-1P 255391-73-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(**chiral** phosphorothioate-linked **oligonucleotides** and their synthesis and use in diagnosis and therapy)

IT 80619-02-9, 5-Lipoxygenase 141436-78-4, Protein kinase C
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(regulation of cellular production of; **chiral** phosphorothioate-linked **oligonucleotides** and their synthesis and use in diagnosis and therapy)

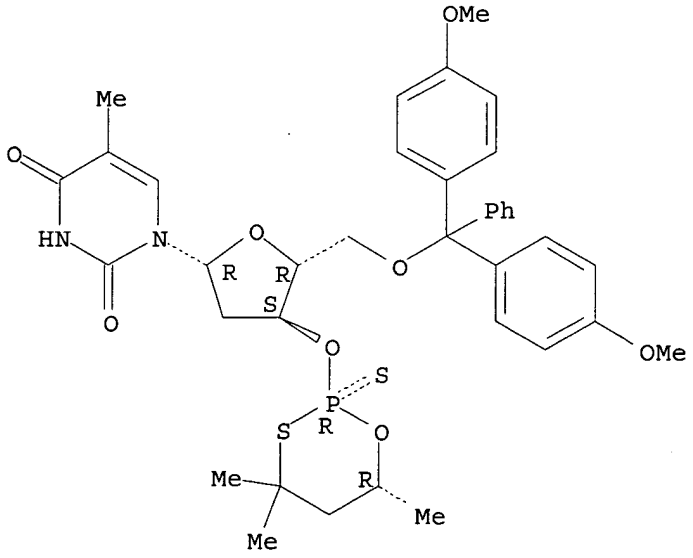
IT 181988-70-5, 6: PN: WO0004034 SEQID: 6 unclaimed DNA
RL: PRP (Properties)
(unclaimed **nucleotide** sequence; **Chiral** phosphorothioate-linked **oligonucleotides** and their synthesis and use in diagnosis and therapy)

IT 181982-21-8, 2: PN: WO0004034 SEQID: 2 unclaimed DNA 181988-09-0, 1: PN: WO0004034 SEQID: 1 unclaimed DNA 186071-78-3 186108-29-2, 10: PN: WO9960167 SEQID: 9 unclaimed DNA 186108-31-6, 3: PN: WO0004034 SEQID: 3 unclaimed DNA
RL: PRP (Properties)
(unclaimed **nucleotide** sequence; **chiral** phosphorothioate-linked **oligonucleotides** and their synthesis and use in diagnosis and therapy)

IT **255391-66-3P 255391-67-4P 255391-69-6P 255391-70-9P 255391-72-1P 255391-73-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**chiral** phosphorothioate-linked **oligonucleotides** and their synthesis and use in diagnosis and therapy)

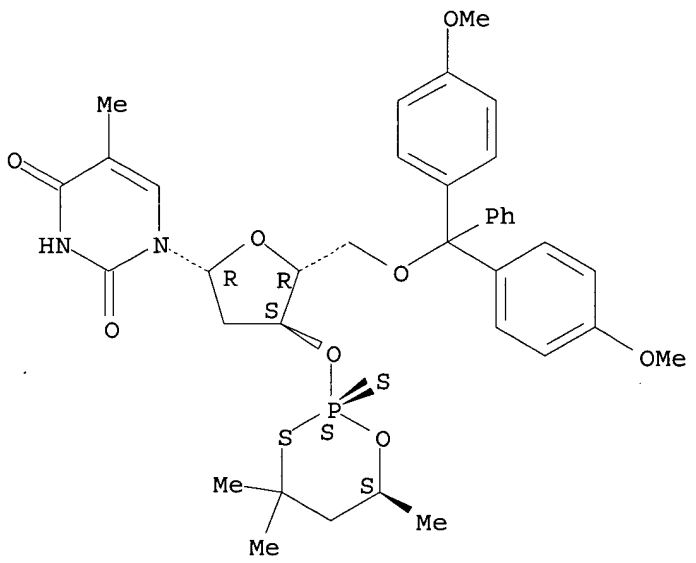
RN 255391-66-3 HCAPLUS
CN Thymidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-3'-O-[(2R,6R)-4,4,6-trimethyl-2-sulfido-1,3,2-oxathiaphosphorinan-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



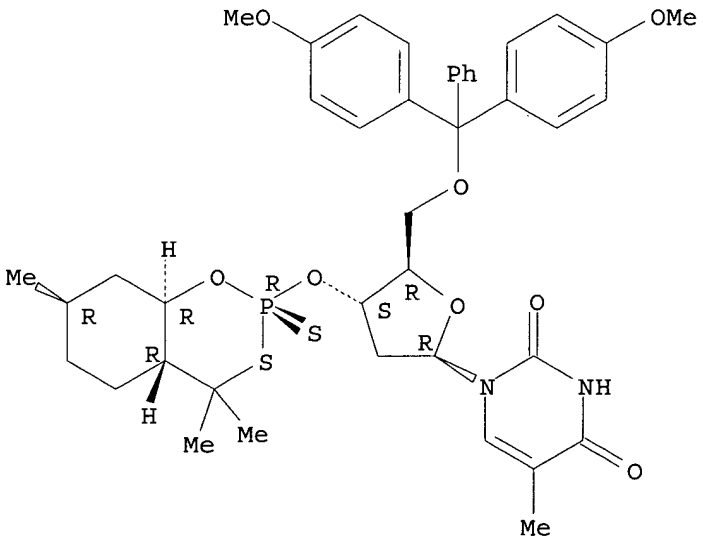
RN 255391-67-4 HCAPLUS
CN Thymidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-3'-O-[(2S,6S)-4,4,6-trimethyl-2-sulfido-1,3,2-oxathiaphosphorinan-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



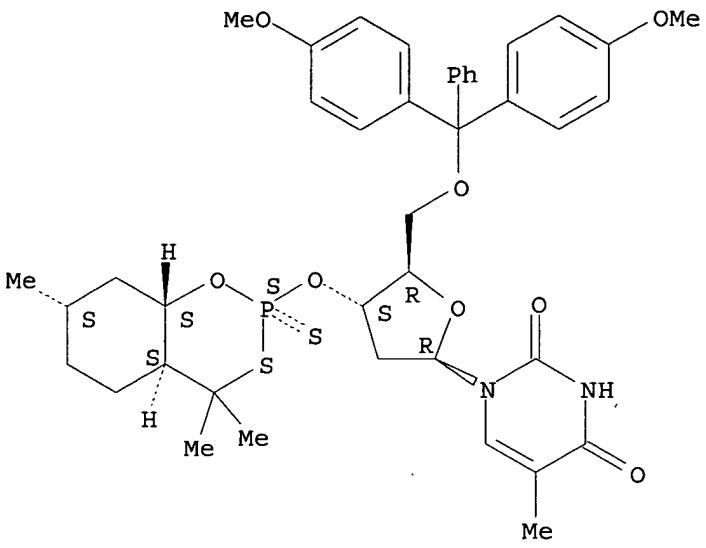
RN 255391-69-6 HCAPLUS
CN Thymidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-3'-O-[(2R,4aR,7R,8aR)-hexahydro-4,4,7-trimethyl-2-sulfido-4H-1,3,2-benzoxathiaphosphorin-2-yl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



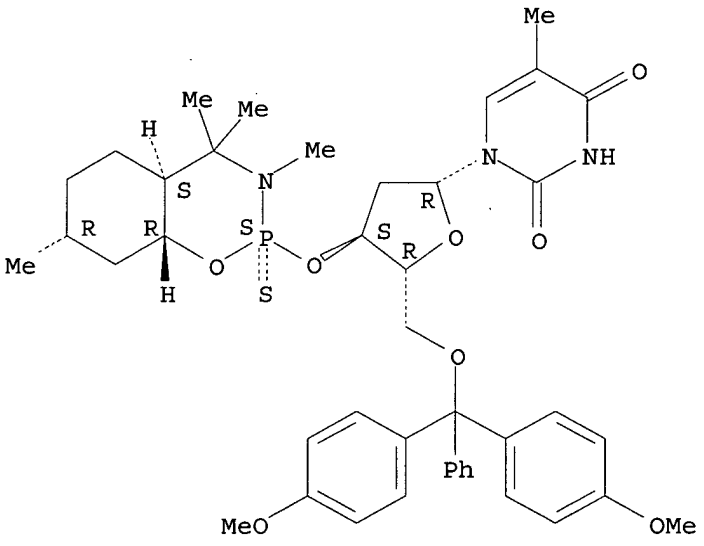
RN 255391-70-9 HCAPLUS
CN Thymidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-3'-O-[(2S,4aS,7S,8aS)-hexahydro-4,4,7-trimethyl-2-sulfido-4H-1,3,2-benzoxathiaphosphorin-2-yl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



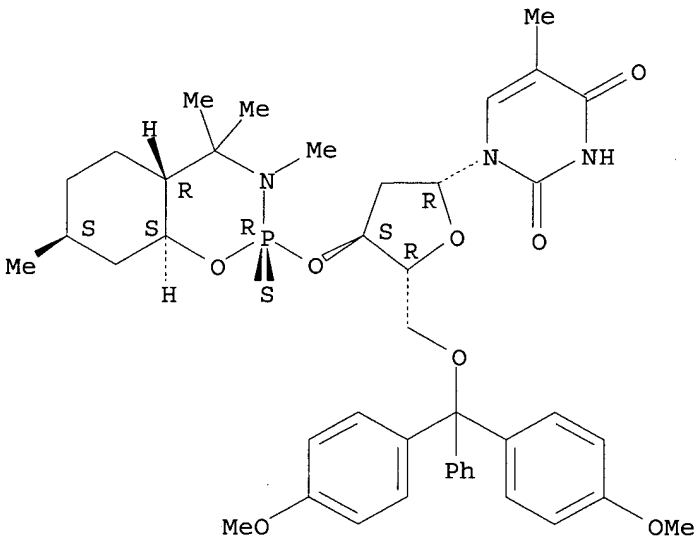
RN 255391-72-1 HCAPLUS
CN Thymidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-3'-O-[(2S,4aS,7R,8aR)-octahydro-3,4,4,7-tetramethyl-2-sulfido-2H-1,3,2-benzoxaazaphosphorin-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 255391-73-2 HCAPLUS
CN Thymidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-3'-O-[(2R,4aR,7S,8aS)-octahydro-3,4,4,7-tetramethyl-2-sulfido-2H-1,3,2-benzoxaazaphosphorin-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 18 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:121638 HCAPLUS
DOCUMENT NUMBER: 132:177252
TITLE: **Oligonucleotides** with **chirally** pure phosphonate- mixed with non-phosphonate **internucleosidyl** linkages and their use in inhibition of protein synthesis
INVENTOR(S): Arnold, Lyle John, Jr.; Hogrefe, Richard Isais; Reynolds, Mark Alan; Riley, Timothy Andrew; Schwartz, David Aaron; Vaghefi, Morteza Monir; Brown, Bob Dale
PATENT ASSIGNEE(S): Genta Incorporated, USA
SOURCE: U.S., 40 pp., Cont.-in-part of U.S. Ser. No. 154,014.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 6028188	A	20000222	US 1994-342924		19941121
IL 128658	A1	20030312	IL 1994-128658		19941116
US 5792615	A	19980811	US 1997-812861		19970306
US 6060456	A	20000509	US 1997-960111		19971027
PRIORITY APPLN. INFO.:			US 1993-154014	A2	19931116
			US 1993-154013	A	19931116
			US 1994-233778	A	19940426
			US 1994-238177	A	19940504
			IL 1994-111660	A3	19941116
			US 1995-481637	B1	19950607

OTHER SOURCE(S): MARPAT 132:177252
ED Entered STN: 22 Feb 2000
AB Oligomers having **chirally** pure phosphonate **internucleosidyl** linkages mixed with non-phosphonate **internucleosidyl** linkages which hybridize to RNA target sequences and methods for their preparation are provided. The **oligonucleotides** are prepared by linking together dimer, trimer, and/or tetramer synthons

containing **chiral** phosphonate **internucleoside** linkages. Thus, several **oligonucleotides** with alternating phosphodiester-Rp methylphosphonate linkages were synthesized and the increased Tm and resistance to nuclease degradation in vitro and in vivo were demonstrated. One of these **oligonucleotide** analogs was shown to inhibit splicing/protein synthesis in a COS-7 cell model system.

IC ICM C07H021-04
INCL 536025300
CC 6-2 (General Biochemistry)
Section cross-reference(s): 3
ST **oligonucleotide chiral** phosphonate phosphodiester linked synthesis translation inhibition
IT RNA splicing
(inhibition of; **oligonucleotides** with **chirally** pure phosphonate- mixed with non-phosphonate **internucleosidyl** linkages and their use in inhibition of protein synthesis)
IT mRNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**oligonucleotides** binding to; **oligonucleotides** with **chirally** pure phosphonate- mixed with non-phosphonate **internucleosidyl** linkages and their use in inhibition of protein synthesis)
IT **Translation, genetic**
(**oligonucleotides** with **chirally** pure phosphonate- mixed with non-phosphonate **internucleosidyl** linkages and their use in inhibition of protein synthesis)
IT **Antisense oligonucleotides**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**oligonucleotides** with **chirally** pure phosphonate- mixed with non-phosphonate **internucleosidyl** linkages and their use in inhibition of protein synthesis)
IT 259164-71-1P 259164-72-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(**oligonucleotides** with **chirally** pure phosphonate- mixed with non-phosphonate **internucleosidyl** linkages and their use in inhibition of protein synthesis)
IT 168758-24-5P 168758-25-6P 168758-26-7P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(**oligonucleotides** with **chirally** pure phosphonate- mixed with non-phosphonate **internucleosidyl** linkages and their use in inhibition of protein synthesis)
IT 2140-71-8, 2'-O-Methylguanosine **2140-72-9**, 2'-O-Methylcytidine **40733-27-5** 51747-24-1 58479-61-1 **103285-22-9** 114745-26-5 **128192-22-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(**oligonucleotides** with **chirally** pure phosphonate- mixed with non-phosphonate **internucleosidyl** linkages and their use in inhibition of protein synthesis)
IT **168635-65-2P 168635-66-3P 168635-68-5P 168635-69-6P 168635-71-0P 168635-72-1P** 168635-73-2P 168635-74-3P 168635-75-4P **168635-77-6P 168635-78-7P** 168635-79-8P **168635-80-1P 168635-81-2P 168635-82-3P 168635-83-4P 168752-52-1P 168752-53-2P 168752-54-3P** 168752-55-4P **168752-56-5P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**oligonucleotides** with **chirally** pure phosphonate- mixed with non-phosphonate **internucleosidyl** linkages and their use in inhibition of protein synthesis)

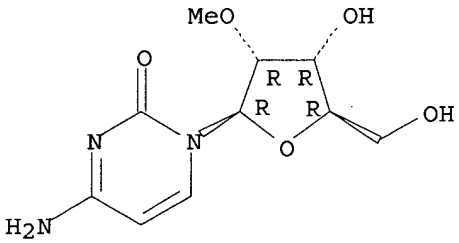
IT 243687-47-0, 1: PN: US6028188 SEQID: 1 unclaimed DNA 243687-49-2, 3: PN: US6028188 SEQID: 4 unclaimed DNA 243687-55-0, 4: PN: US6028188 SEQID: 5 unclaimed DNA 245081-48-5, PN: US5958901 SEQID: 1 unclaimed RNA 245081-49-6, PN: US5958901 SEQID: 2 unclaimed RNA 245081-50-9, PN: US5958901 SEQID: 4 unclaimed RNA 245081-51-0, PN: US5958901 SEQID: 6 unclaimed RNA 259128-15-9, 24: PN: US6028188 SEQID: 2 unclaimed DNA 259128-16-0, 2: PN: US6028188 SEQID: 3 unclaimed DNA 259128-17-1, 9: PN: US6028188 SEQID: 12 unclaimed DNA 259128-18-2 259128-19-3 259128-20-6 259128-21-7 259128-22-8 259128-23-9 259128-24-0 259128-25-1 259128-26-2 259128-27-3 259128-28-4 259128-29-5 259128-30-8
RL: PRP (Properties)
(unclaimed **nucleotide** sequence; **oligonucleotides** with **chirally** pure phosphonate- mixed with non-phosphonate **internucleosidyl** linkages and their use in inhibition of protein synthesis)

IT 245061-65-8 259111-50-7
RL: PRP (Properties)
(unclaimed sequence; **oligonucleotides** with **chirally** pure phosphonate- mixed with non-phosphonate **internucleosidyl** linkages and their use in inhibition of protein synthesis)

IT **2140-72-9**, 2'-O-Methylcytidine **40733-27-5** **103285-22-9** **128192-22-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(**oligonucleotides** with **chirally** pure phosphonate- mixed with non-phosphonate **internucleosidyl** linkages and their use in inhibition of protein synthesis)

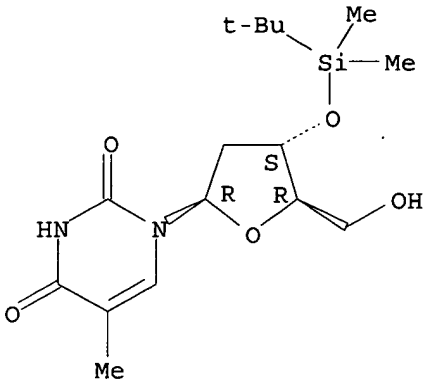
RN 2140-72-9 HCAPLUS
CN Cytidine, 2'-O-methyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



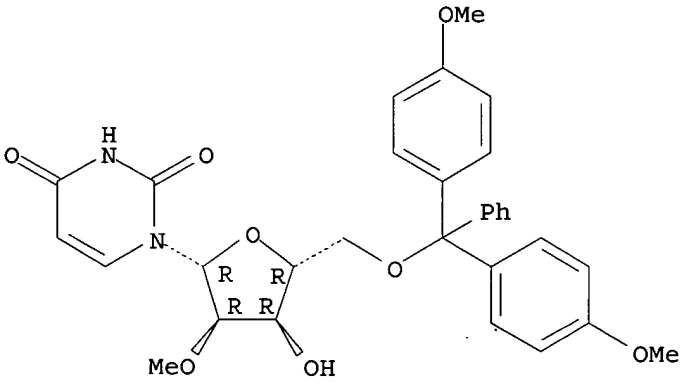
RN 40733-27-5 HCAPLUS
CN Thymidine, 3'-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



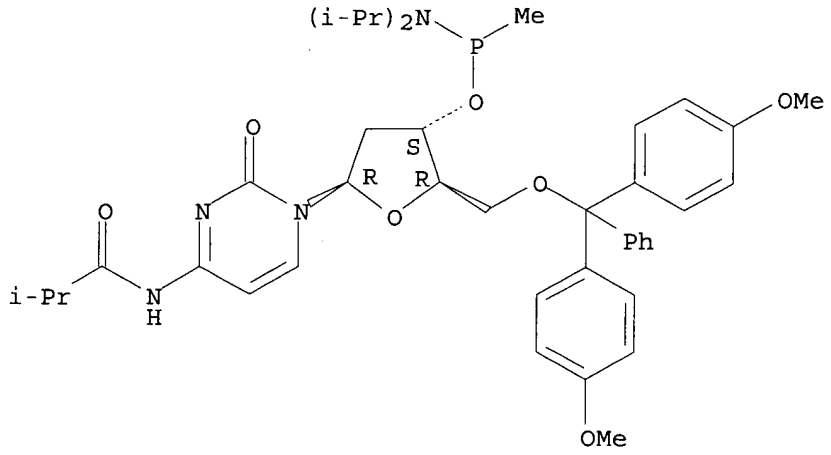
RN 103285-22-9 HCAPLUS
CN Uridine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 128192-22-3 HCAPLUS
CN Cytidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-N-(2-methyl-1-oxopropyl)-, 3'-[P-methyl-N,N-bis(1-methylethyl)phosphonamidite] (9CI) (CA INDEX NAME)

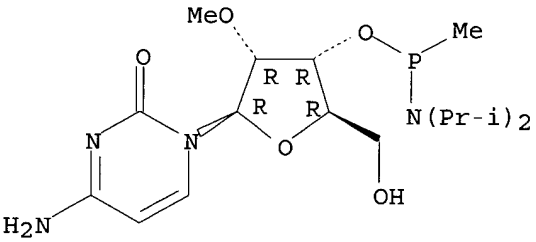
Absolute stereochemistry.



IT **168635-65-2P 168635-66-3P 168635-68-5P**
168635-69-6P 168635-71-0P 168635-72-1P
168635-77-6P 168635-78-7P 168635-80-1P
168635-81-2P 168635-82-3P 168635-83-4P
168752-52-1P 168752-53-2P 168752-54-3P
168752-56-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**oligonucleotides** with **chirally** pure phosphonate-mixed with non-phosphonate **internucleosidyl** linkages and their use in inhibition of protein synthesis)

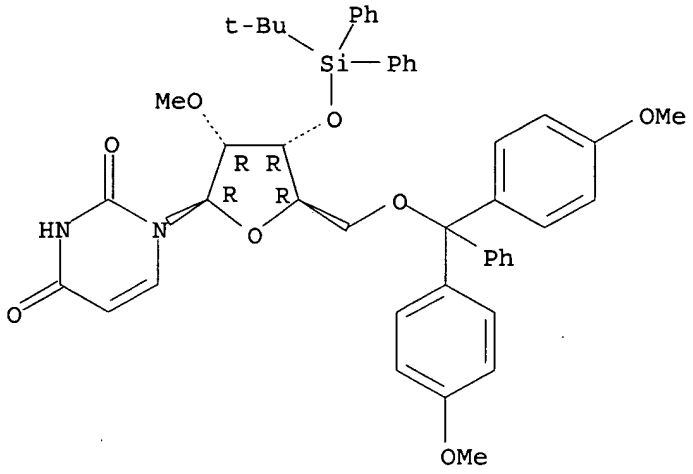
RN 168635-65-2 HCAPLUS
CN Cytidine, 2'-O-methyl-, 3'-[P-methyl-N,N-bis(1-methylethyl)phosphonamidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



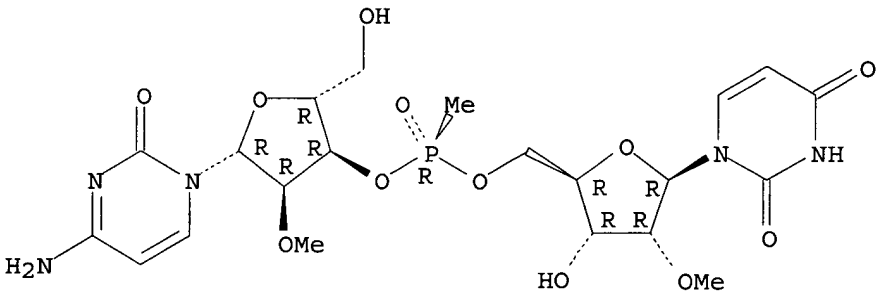
RN 168635-66-3 HCAPLUS
CN Uridine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-3'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



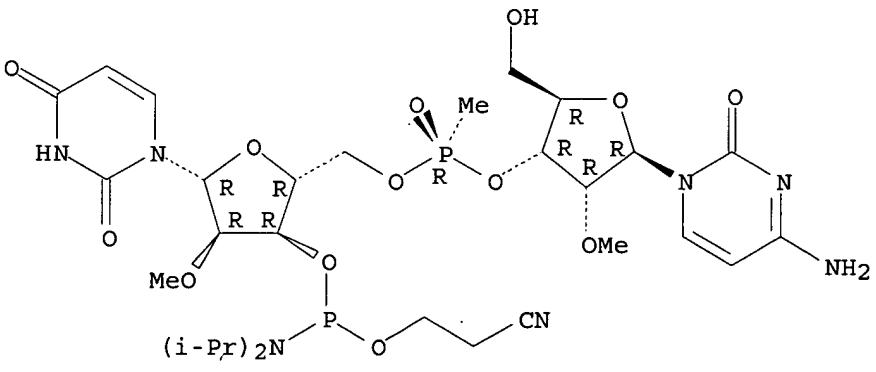
RN 168635-68-5 HCAPLUS
CN Uridine, (R)-P-deoxy-P-methyl-2'-O-methylcytidylyl-(3'→5')-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



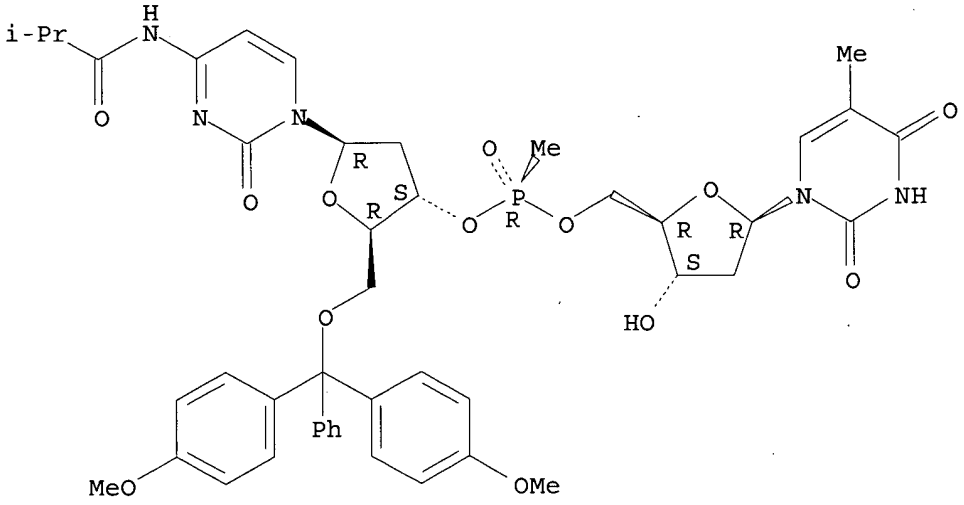
RN 168635-69-6 HCAPLUS
CN Uridine, (R)-P-deoxy-P-methyl-2'-O-methylcytidylyl-(3'→5')-2'-O-methyl-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



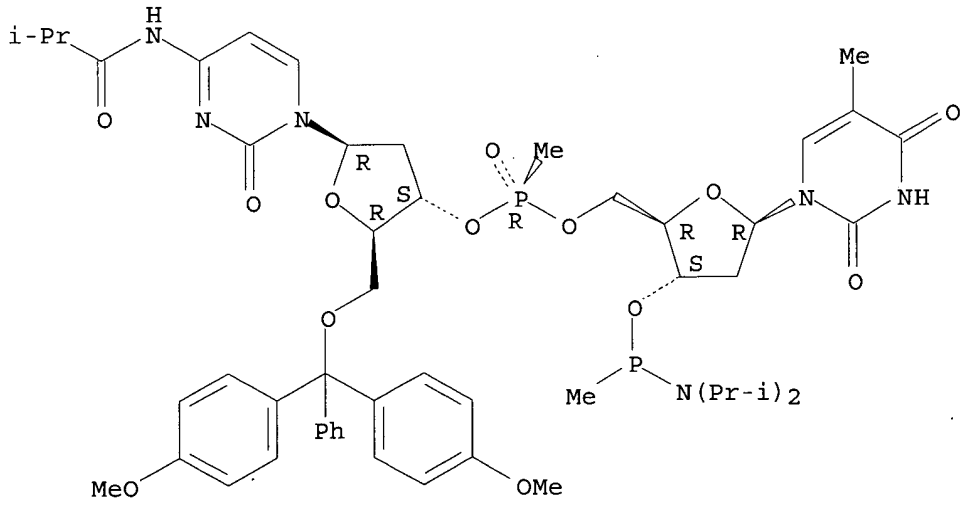
RN 168635-71-0 HCAPLUS
CN Thymidine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P,2'-dideoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



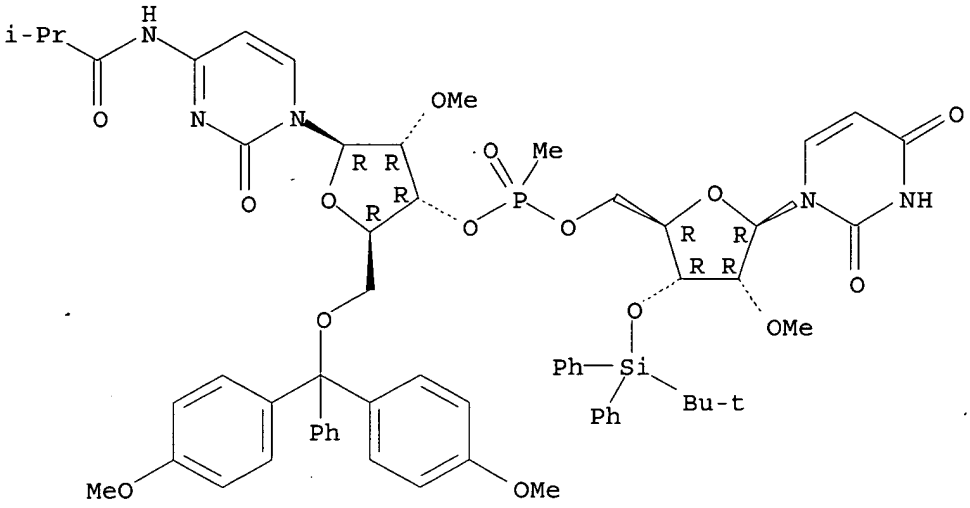
RN 168635-72-1 HCAPLUS
CN Thymidine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P,2'-dideoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-, 3'-[P-methyl-N,N-bis(1-methylethyl)phosphonamidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



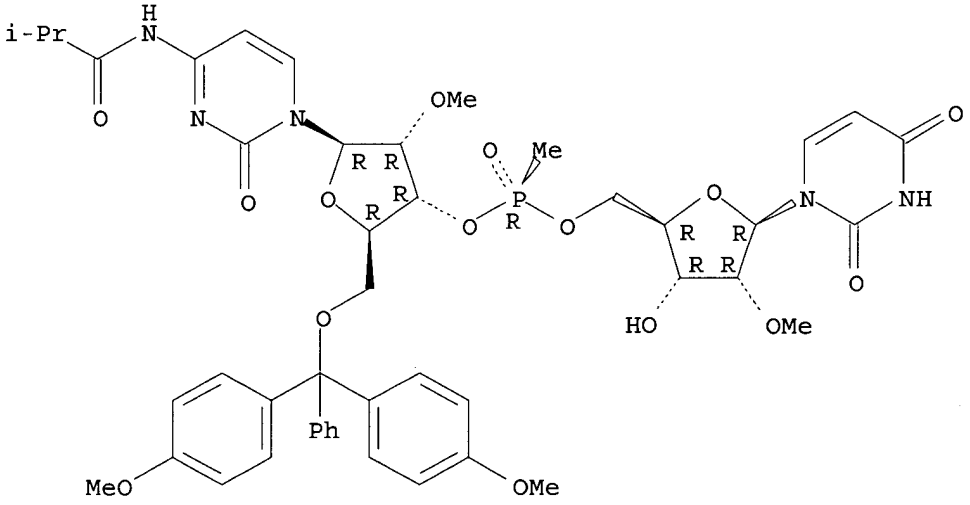
RN 168635-77-6 HCAPLUS
CN Uridine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-2'-O-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-3-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



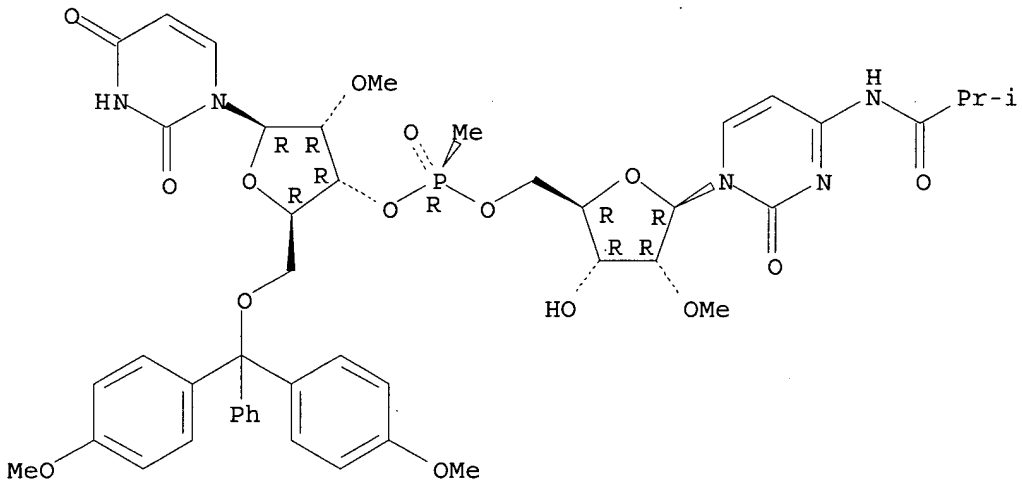
RN 168635-78-7 HCAPLUS
CN Uridine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-2'-O-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



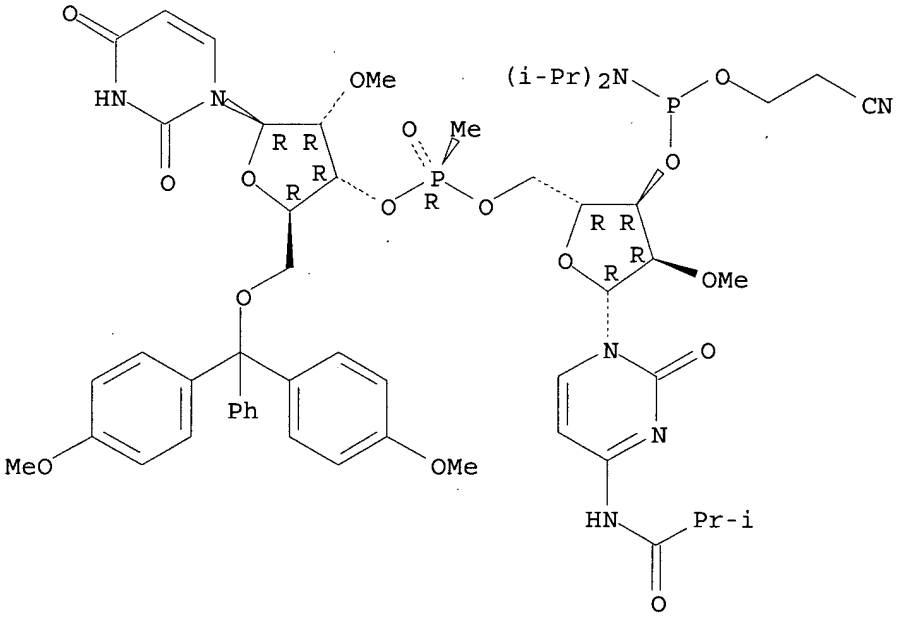
RN 168635-80-1 HCAPLUS
CN Cytidine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-2'-O-methyluridylyl-(3'→5')-2'-O-methyl-N-(2-methyl-1-oxopropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



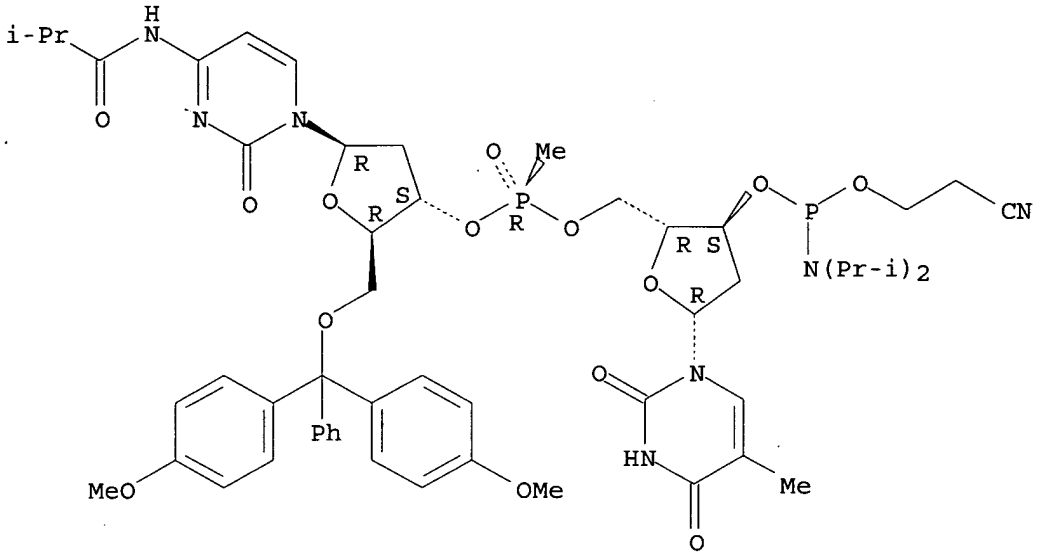
RN 168635-81-2 HCAPLUS
CN Cytidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-2'-O-methyluridylyl-(3'→5')-2'-O-methyl-N-(2-methyl-1-oxopropyl)-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



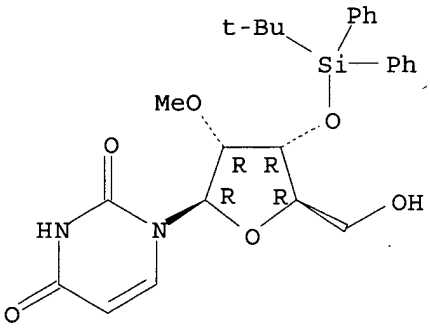
RN 168635-82-3 HCAPLUS
CN Thymidine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P,2'-dideoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



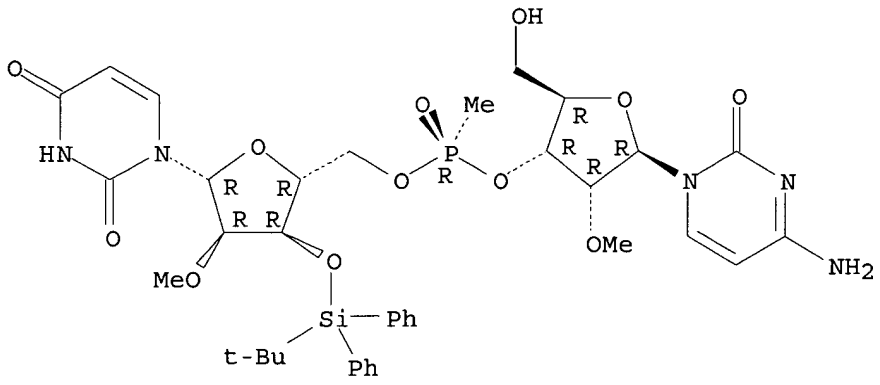
RN 168635-83-4 HCAPLUS
CN Uridine, 3'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



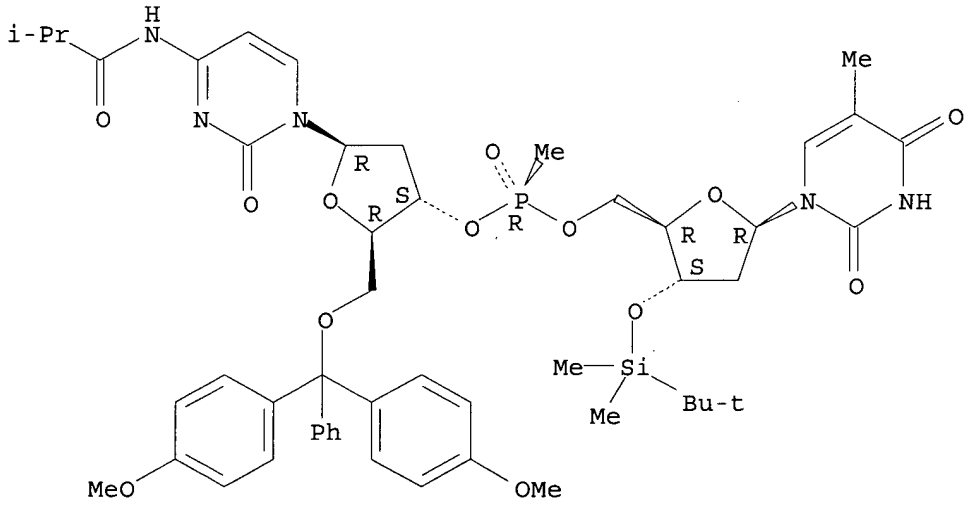
RN 168752-52-1 HCAPLUS
CN Uridine, (R)-P-deoxy-P-methyl-2'-O-methylcytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)diphenylsilyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



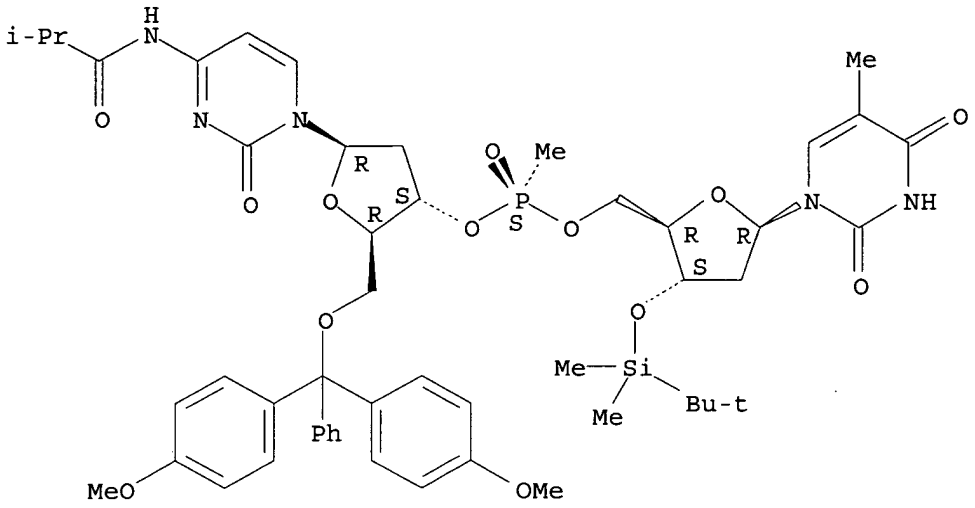
RN 168752-53-2 HCAPLUS
CN Thymidine, [P(R)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



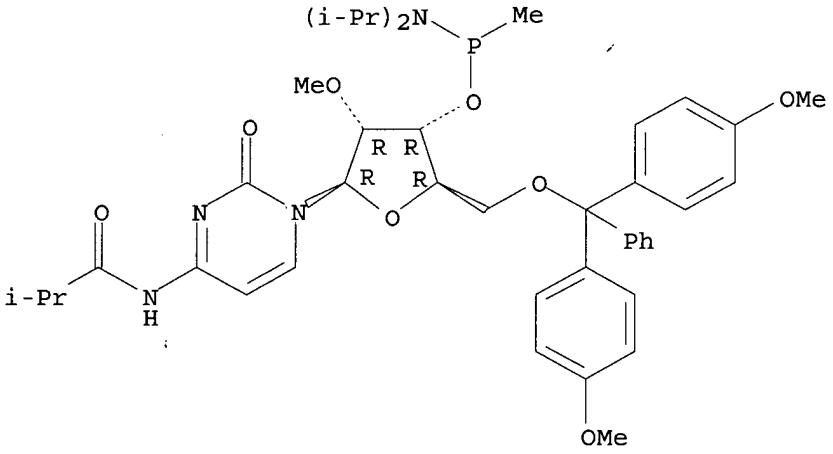
RN 168752-54-3 HCAPLUS
CN Thymidine, [P(S)]-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-P-deoxy-P-methyl-N-(2-methyl-1-oxopropyl)cytidylyl-(3'→5')-3'-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 168752-56-5 HCAPLUS
CN Cytidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyl-N-(2-methyl-1-oxopropyl)-, 3'-[P-methyl-N,N-bis(1-methylethyl)phosphonamidate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 19 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:633824 HCAPLUS
DOCUMENT NUMBER: 133:203448
TITLE: Phage displays of ScFv peptides recognizing the thymidine(6-4)thymidine photoproduct
AUTHOR(S): Zavala, Anamaria G.; Lancaster, Thaddeus; Groopman, John D.; Strickland, Paul T.; Chandrasegaran, Srinivasan
CORPORATE SOURCE: Department of Environmental Health Sciences, The Johns Hopkins University School of Public Health, Baltimore, MD, 21205-2719, USA

SOURCE: Nucleic Acids Research (2000), 28(7), e24, ii-vii
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 13 Sep 2000

AB Solar UV radiation induces DNA photo-products in skin cells and is the predominant cause of human skin cancers. To understand human susceptibility to skin cancer and to facilitate the development of prevention measures, highly specific reagents to detect and quantitate UV-induced DNA adducts in human skin will be needed. One approach towards this end is the use of monoclonal antibody-based mol. dosimetry methods. To facilitate the development of photoproduct-specific antibody reagents we have: (i) cloned and sequenced a single chain variable fragment (ScFv) gene coding for one such highly affinity monoclonal antibody, αUVssDNA-1 (mAb C3B6), recognizing the thymidine(6-4)thymidine photoproduct; (ii) **expressed** and displayed the cloned ScFv **gene** on the surface of phage; (iii) selected functional recombinant phage by panning; (iv) purified the ScFv peptide; (v) shown that the purified ScFv peptide binds to UV-irradiated polythymidylic acid but not unirradiated polythymidylic acid. This is the first demonstration of the use of phage display to select a ScFv recognizing DNA damage. In addition, this is the initial step towards immortalizing the antibody gene for genetic manipulation, structure-function studies and application to human investigations.

CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 15

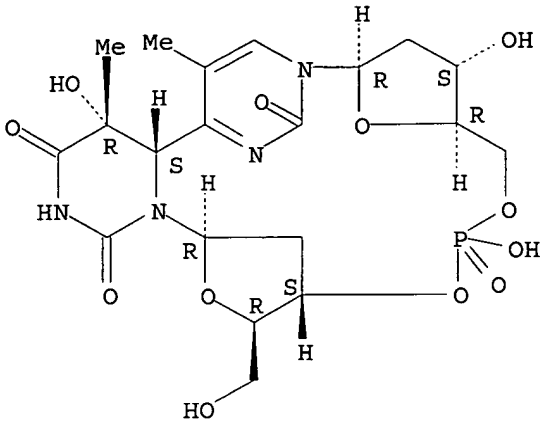
IT **100850-36-0**
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(phage displays of ScFv peptides recognizing the thymidine(6-4)thymidine photoproduct)

IT **100850-36-0**
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(phage displays of ScFv peptides recognizing the thymidine(6-4)thymidine photoproduct)

RN 100850-36-0 HCAPLUS

CN 3'-Thymidylic acid, 6-[1-(2-deoxy-β-D-erythro-pentofuranosyl)-1,2-dihydro-5-methyl-2-oxo-4-pyrimidinyl]-5,6-dihydro-5-hydroxy-, intramol. 3',5'''-ester, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 20 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:367752 HCAPLUS
DOCUMENT NUMBER: 129:105202
TITLE: **Chirally** modified **oligonucleotides** and the control of **gene expression** The case of L-DNAs and -RNAs
AUTHOR(S): Garbesi, Anna; Capobianco, Massimo L.; Colonna, Francesco P.; Maffini, Mauro; Niccolai, Daniela; Tondelli, Luisa
CORPORATE SOURCE: ICoCEA, Consiglio Nazionale delle Ricerche, Bologna, 40129, Italy
SOURCE: Nucleosides & Nucleotides (1998), 17(7), 1275-1287
CODEN: NUNUD5; ISSN: 0732-8311
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 17 Jun 1998
AB The affinity of L-DNAs, L-RNAs and L/D-DNAs for homopurine•homopyrimidine d.s. D-DNA and s.s. D-RNA was probed by gel electrophoresis and CD spectroscopy. It was found that the L-modified oligomers do not bind to d.s. DNA and to natural RNA that contains all four natural bases. Thus they cannot be used, in **general**, for the control of **gene expression** according to the **antigene** and antisense methodologies. Heterochiral complexes with 1:1 stoichiometry and low thermal stability are formed, instead, by homopurinic L-RNA or L/D-DNA and homopyrimidinic L-RNA with the W/C complementary natural RNA sequences.
CC 3-6 (Biochemical Genetics)
ST **chirally** modified **oligonucleotides** regulation **gene expression**; L DNA RNA expression **chiral oligonucleotides**
IT RNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D-, single-stranded, L-modified oligomers do not bind to D-RNA; **chirally** modified **oligonucleotides** and the control of **gene expression**: the case of L-DNAs and -RNAs)
IT DNA
RNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(L-; **chirally** modified **oligonucleotides** and the control of **gene expression**: the case of L-DNAs and -RNAs)

IT **Oligonucleotides**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**chirally** modified; **chirally** modified **oligonucleotides** and the control of **gene expression**: the case of L-DNAs and -RNAs)

IT DNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(double-stranded, homopurine•homopyrimidine D-DNA, L-modified oligomers do not bind to d.s. DNA; **chirally** modified **oligonucleotides** and the control of **gene expression**: the case of L-DNAs and -RNAs)

IT Gene
(regulation; **chirally** modified **oligonucleotides** and the control of **gene expression**: the case of L-DNAs and -RNAs)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 21 OF 84 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:837554 HCAPLUS
DOCUMENT NUMBER: 123:248529
TITLE: **Chirally** enriched synthetic phosphonate **oligonucleotides**: their preparation and use in preventing formation or translation of RNA
INVENTOR(S): Arnold, Lyle John, Jr.; Reynolds, Mark Alan; Riley, Timothy Andrew; Schwartz, David Aaron; Vaghefi, Morteza Monir
PATENT ASSIGNEE(S): Genta, Inc., USA
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9514031	A1	19950526	WO 1994-US13395	19941116
W: AU, CA, JP, KR, NZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2176372	AA	19950526	CA 1994-2176372	19941116
AU 9511834	A1	19950606	AU 1995-11834	19941116
AU 695552	B2	19980813		
EP 731809	A1	19960918	EP 1995-902633	19941116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09505307	T2	19970527	JP 1994-514650	19941116
IL 128658	A1	20030312	IL 1994-128658	19941116
TW 390884	B	20000521	TW 1994-83111152	19941130
US 5837856	A	19981117	US 1997-814053	19970306
US 5955597	A	19990921	US 1997-885126	19970630
US 6060456	A	20000509	US 1997-960111	19971027

PRIORITY APPLN. INFO.:

US 1993-154013	A	19931116
US 1993-154014	A	19931116
US 1994-233778	A	19940426
US 1994-238177	A	19940504
IL 1994-111660	A3	19941116

WO 1994-US13395 W 19941116
US 1994-343018 B1 19941121
US 1995-481637 B1 19950607

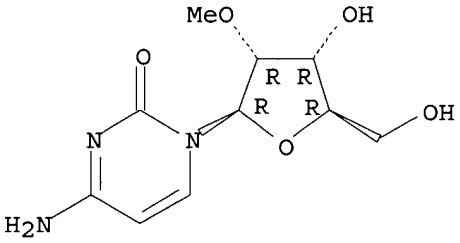
OTHER SOURCE(S): MARPAT 123:248529
ED Entered STN: 07 Oct 1995
AB Oligomers having phosphonate **internucleosidyl** linkages which are enriched for phosphonate linkages of a preselected **chirality** which hybridize to an RNA target sequence and methods for their preparation are provided. **Dinucleotide** synthons containing Rp methylphosphonate linkages and **oligonucleotides** containing these synthons were prepared These **oligonucleotides** bound more tightly to target nucleic acids than did **oligonucleotides** containing racemic methylphosphonate linkages. **Oligonucleotides** with Rp methylphosphonate linkages inhibited protein formation in in vitro systems more effectively than the racemic analogs.
IC ICM C07H021-04
ICS A61K048-00
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 33
ST **oligonucleotide chiral** methylphosphonate linkage synthesis; RNA biosynthesis translation methylphosphonate linked **oligonucleotide**
IT **Transcription, genetic**
Translation, genetic
(inhibition of; preparation and use in preventing formation or translation of RNA of **chirally** enriched synthetic phosphonate **oligonucleotides**)
IT **Nucleotides, biological studies**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**oligo**-, phosphonate-linked, **chirally** enriched; preparation and use in preventing formation or translation of RNA of **chirally** enriched synthetic phosphonate **oligonucleotides**)
IT **Nucleotides, biological studies**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**oligo**-, methylphosphonate-linked, **chirally** enriched; preparation and use in preventing formation or translation of RNA of **chirally** enriched synthetic phosphonate **oligonucleotides**)
IT 168758-14-3P 168758-15-4P 168758-16-5P 168758-17-6P 168758-18-7P
168758-19-8P 168758-20-1P 168758-21-2P 168758-22-3P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and use in preventing formation or translation of RNA of **chirally** enriched synthetic phosphonate **oligonucleotides**)
IT **2140-72-9**, 2'-O-Methyl cytidine **40733-27-5** 51747-24-1
58479-61-1 **103285-22-9 128192-22-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and use in preventing formation or translation of RNA of **chirally** enriched synthetic phosphonate **oligonucleotides**)
IT **168635-65-2P 168635-66-3P 168635-67-4P**
168635-68-5P 168635-70-9P 168635-71-0P
168635-72-1P 168635-83-4P 168635-84-5P
168752-52-1P 168752-53-2P 168752-54-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and use in preventing formation or translation of RNA of

chirally enriched synthetic phosphonate **oligonucleotides**)

IT **2140-72-9**, 2'-O-Methyl cytidine **40733-27-5** **103285-22-9** **128192-22-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and use in preventing formation or translation of RNA of **chirally** enriched synthetic phosphonate **oligonucleotides**)

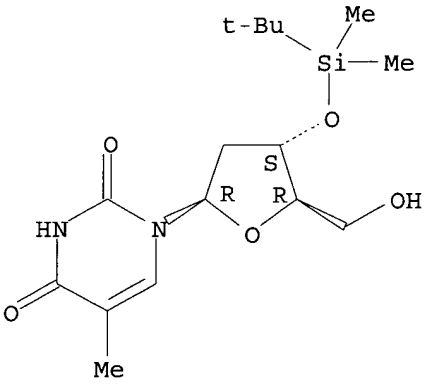
RN 2140-72-9 HCAPLUS
CN Cytidine, 2'-O-methyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



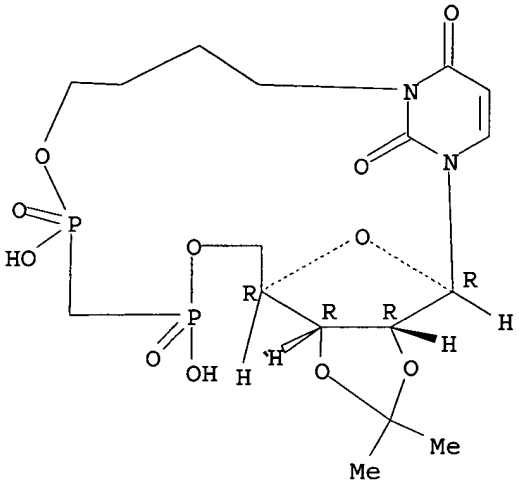
RN 40733-27-5 HCAPLUS
CN Thymidine, 3'-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



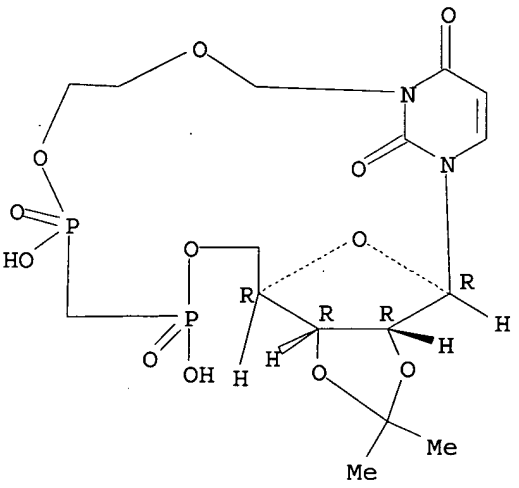
RN 103285-22-9 HCAPLUS
CN Uridine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



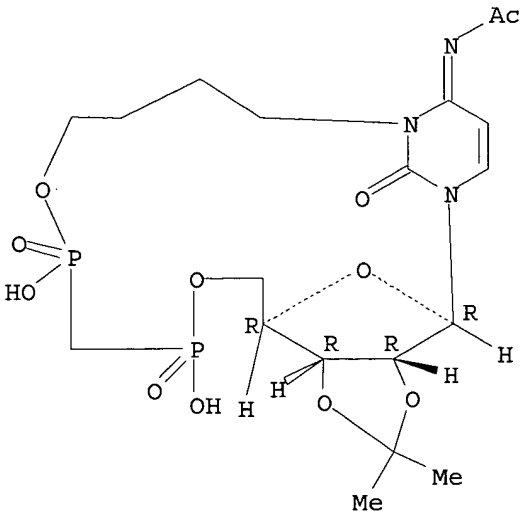
RN 206544-53-8 USPATFULL
CN Uridine, 2',3'-O-(1-methylethylidene)-3-(6,8,8-trihydroxy-6,8-dioxido-2,5-dioxa-6,8-diphosphaoct-1-yl)-, intramol. P'→5'-ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



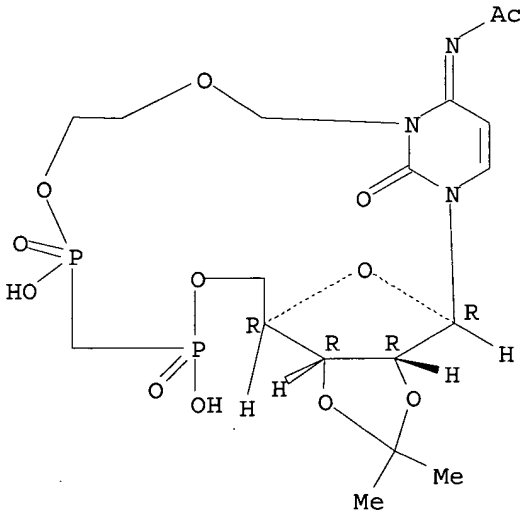
RN 206647-82-7 USPATFULL
CN Cytidine, N-acetyl-3-[4-[[hydroxy(phosphonomethyl)phosphinyl]oxy]butyl]-2',3'-O-(1-methylethylidene)-, intramol. P'→5'-ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 206647-83-8 USPATFULL
CN Cytidine, N-acetyl-2',3'-O-(1-methylethylidene)-3-(6,8,8-trihydroxy-6,8-dioxido-2,5-dioxa-6,8-diphosphaoct-1-yl)-, intramol. P'→5'-ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



L89 ANSWER 59 OF 84 USPATFULL on STN
ACCESSION NUMBER: 1999:24784 USPATFULL
TITLE: Coupling unit of (6-4) photoproduct, process for preparing the same, process for preparing oligonucleotide containing (6-4) photoproduct by using the same and process for preparing DNA containing (6-4) photoproduct by using the same
INVENTOR(S): Iwai, Shigenori, Osaka, Japan
PATENT ASSIGNEE(S): Biomolecular Engineering Research Institute, Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5874568		19990223
APPLICATION INFO.:	US 1997-783986		19970115 (8)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1996-15236	19960131
	JP 1996-136272	19960530

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Knode, Marian C.
ASSISTANT EXAMINER: Crane, L. Eric
LEGAL REPRESENTATIVE: Jordan and Hamburg
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1,3,4,10,12
LINE COUNT: 686
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A coupling unit of a (6-4) photoproduct represented by the formula (I): ##STR1## wherein R.sup.1 represents a protective group, R.sup.2 represents a methyl group or a 2-cyanoethyl group, and R.sup.3 represents ##STR2## wherein R.sup.5 represents a methyl group or a 2-cyanoethyl group, and R.sup.6 represents a --N(R')(R") group, a N-morpholino group, a N-pyrrolidinyl group or a 2,2,6,6-tetramethyl-N-piperidyl group where R' and R" each represent a lower alkyl group,

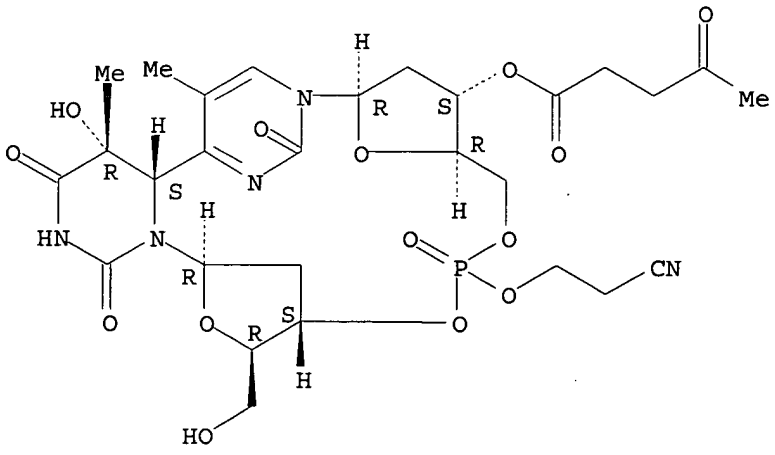
a process for preparing the same, a process for preparing an oligonucleotide containing a (6-4) photoproduct by using the same, and a process for preparing DNA containing a (6-4) photoproduct by using the same are disclosed.

IT **194476-93-2P 194476-94-3P 194476-96-5P**
194541-98-5P
(preparation of photocycloaddn. product oligodeoxyribonucleotides)

RN 194476-93-2 USPATFULL

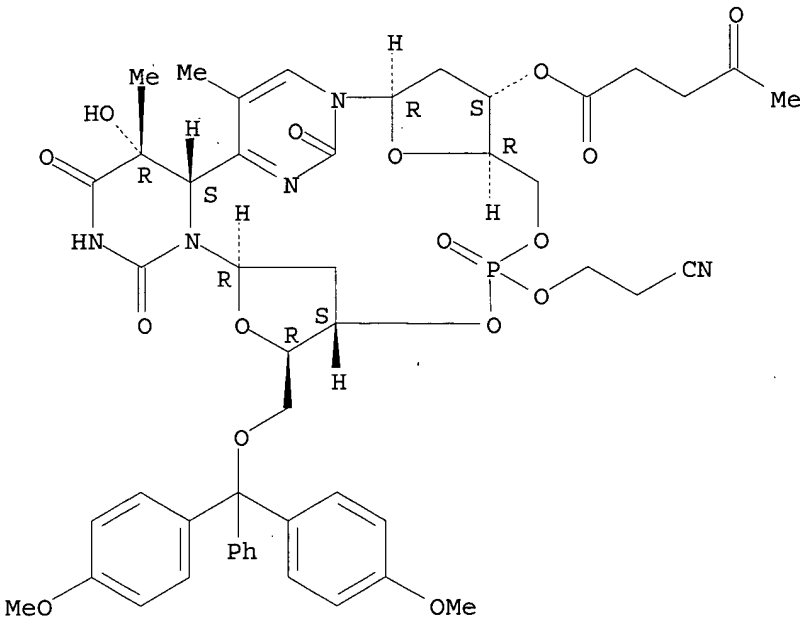
CN 3'-Thymidylic acid, 6-[1-[2-deoxy-3-O-(1,4-dioxopentyl)-β-D-erythro-pentofuranosyl]-1,2-dihydro-5-methyl-2-oxo-4-pyrimidinyl]-5,6-dihydro-5-hydroxy-, mono(2-cyanoethyl) ester, intramol. 3',5'''-ester, (5R,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



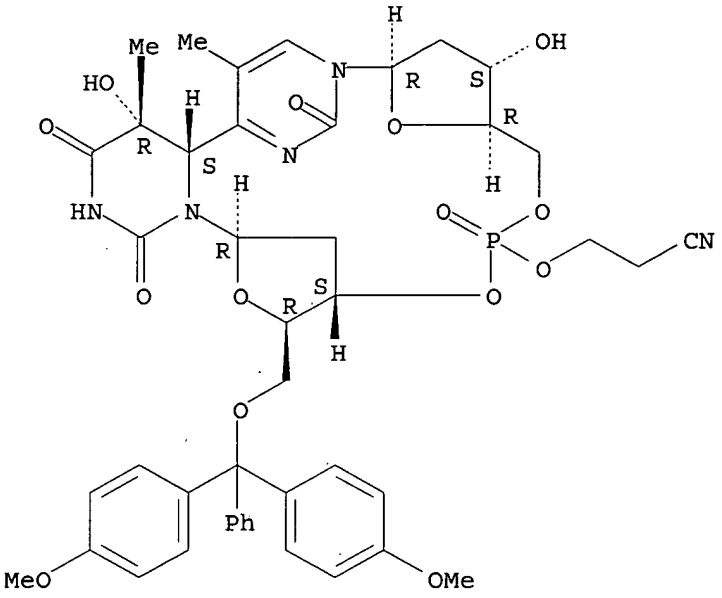
RN 194476-94-3 USPATFULL
CN 3'-Thymidylic acid, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-6-[1-[2-deoxy-3-O-(1,4-dioxopentyl)-β-D-erythro-pentofuranosyl]-1,2-dihydro-5-methyl-2-oxo-4-pyrimidinyl]-5,6-dihydro-5-hydroxy-, mono(2-cyanoethyl) ester, intramol. 3',5'''-ester, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



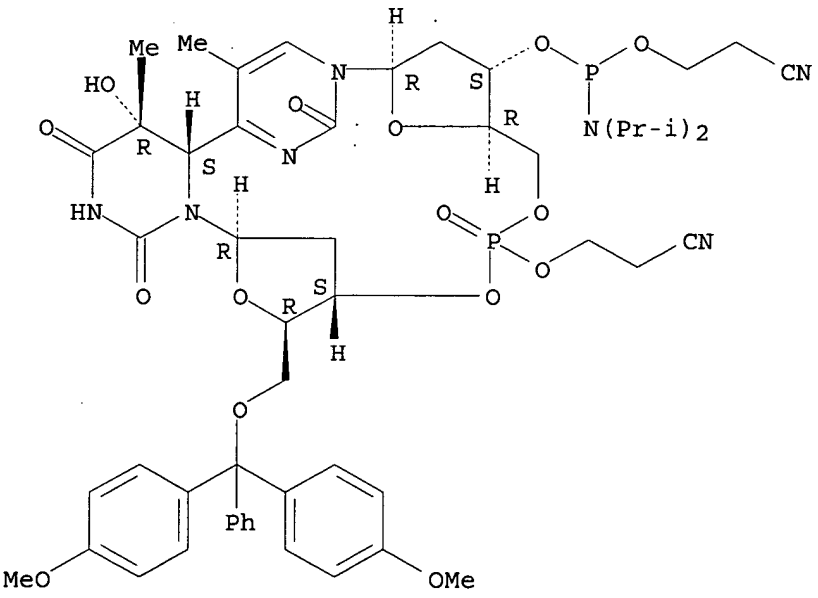
RN 194476-96-5 USPATFULL
CN 3'-Thymidylic acid, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-6-[1-(2-deoxy-β-D-erythro-pentofuranosyl)-1,2-dihydro-5-methyl-2-oxo-4-pyrimidinyl]-5,6-dihydro-5-hydroxy-, mono(2-cyanoethyl) ester, intramol. 3',5'''-ester, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 194541-98-5 USPATFULL
CN 3'-Thymidylic acid, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-6-[1-[3-O-[[bis(1-methylethyl)amino](2-cyanoethoxy)phosphino]-2-deoxy-β-D-erythro-pentofuranosyl]-1,2-dihydro-5-methyl-2-oxo-4-pyrimidinyl]-5,6-dihydro-5-hydroxy-, mono(2-cyanoethyl) ester, intramol. 3',5'''-ester, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

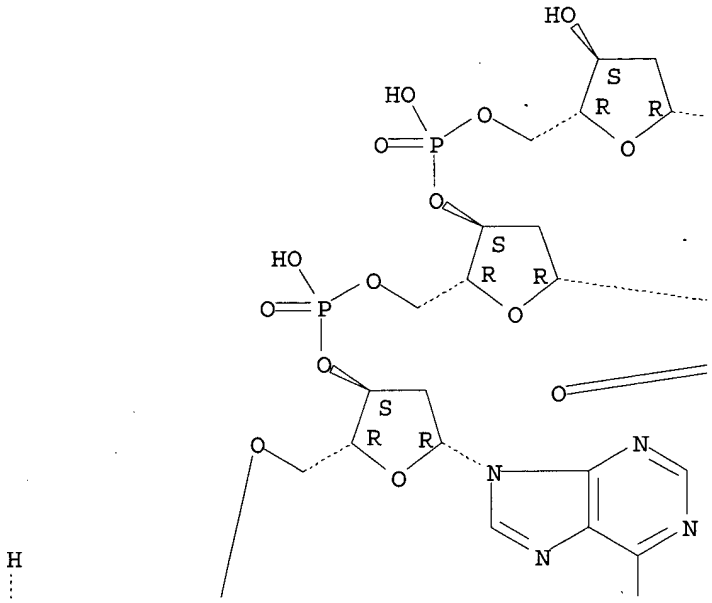


IT **174912-09-5P**
(preparation of photocycloaddn. product oligodeoxyribonucleotides)
RN 174912-09-5 USPATFULL
CN Guanosine, 2'-deoxyguanylyl-(3'→5')-thymidylyl-(3'→5')-2'-

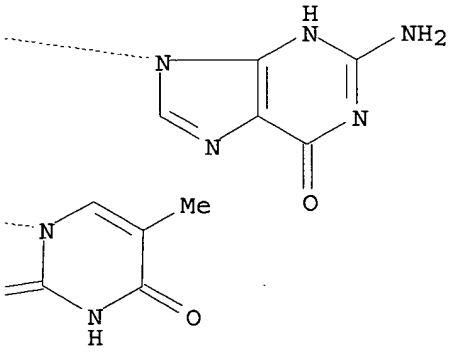
deoxyadenylyl-(3'→5')-[[6,4''-cyclo]-(5R,6S)-5,6-dihydro-5-hydroxythymidylyl-(3'→5')-4-deoxythymidylyl]-(3'→5')-2'-deoxyadenylyl-(3'→5')-thymidylyl-(3'→5')-2'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

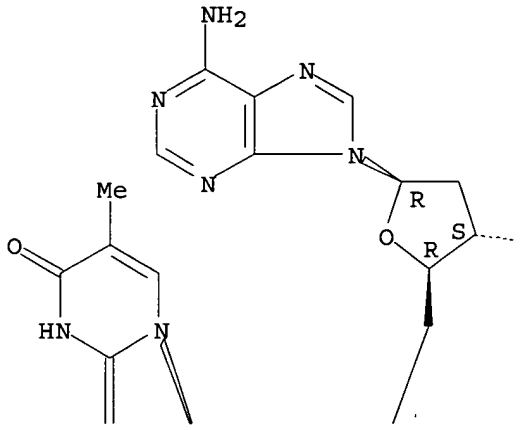
PAGE 1-B



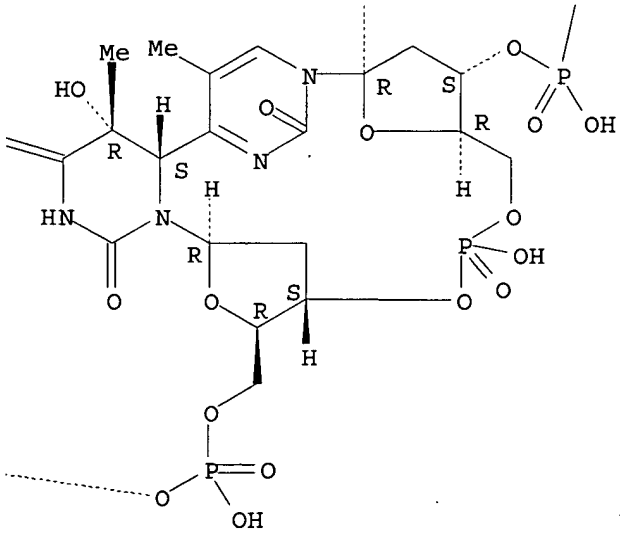
PAGE 1-C



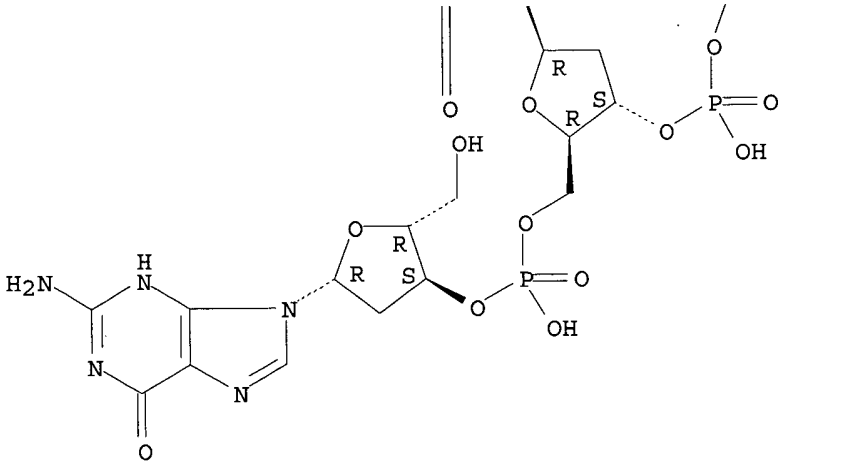
PAGE 2-A



PAGE 2-B



PAGE 3-A



L89 ANSWER 60 OF 84 USPATFULL on STN
ACCESSION NUMBER: 84:63734 USPATFULL
TITLE: Pyrimido (6,1-a)isoquinolin-4-one derivatives
INVENTOR(S): Lal, Bansi, Bombay, India
Dornauer, Horst, Bombay, India
Bhattacharya, Bani K., Bombay, India
Dohadwalla, Alihussein N., Bombay, India
de Souza, Noel J., Bombay, India
PATENT ASSIGNEE(S): Hoechst Aktiengesellschaft, Frankfurt am Main, Germany, Federal Republic of (U.S. corporation)

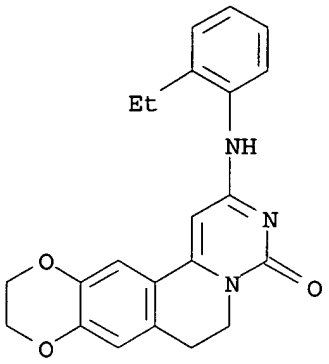
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4482556		19841113
APPLICATION INFO.:	US 1980-134080		19800326 (6)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1977-848289, filed on 3 Nov 1977, now abandoned

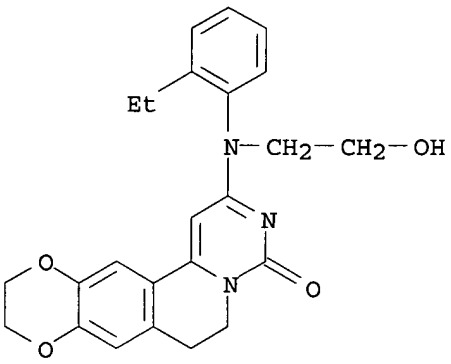
	NUMBER	DATE
PRIORITY INFORMATION:	DE 1977-2720085	19770505

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Hollrah, Glennon H.
ASSISTANT EXAMINER: Turnipseed, James H.
LEGAL REPRESENTATIVE: Curtis, Morris & Safford
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1,12
LINE COUNT: 896
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB What are disclosed are pyrimido (6,1-a)isoquinolin-4-one compounds useful as hypotensive agents, bronchodilators, and anti-allergenics, intermediates useful in their preparation, and methods for making the compounds and intermediates.
IT **94767-67-6P 94767-68-7P**
(preparation of)
RN 94767-67-6 USPATFULL
CN 4H-[1,4]Dioxino[2,3-g]pyrimido[6,1-a]isoquinolin-4-one,

2-[(2-ethylphenyl)amino]-6,7,10,11-tetrahydro- (9CI) (CA INDEX NAME)



RN 94767-68-7 USPATFULL
CN 4H-[1,4]Dioxino[2,3-g]pyrimido[6,1-a]isoquinolin-4-one,
2-[(2-ethylphenyl)(2-hydroxyethyl)amino]-6,7,10,11-tetrahydro- (9CI)
(CA INDEX NAME)



L89 ANSWER 61 OF 84 USPATFULL on STN

ACCESSION NUMBER:	78:27981 USPATFULL
TITLE:	Alkyl triazeno uracil compounds and method of preparation thereof
INVENTOR(S):	Townsend, Leroy B., 3595 Apollo Dr., Salt Lake City, UT, United States 84117 Thurber, T. Craig, 227 S. 13 East, Salt Lake City, UT, United States 84115

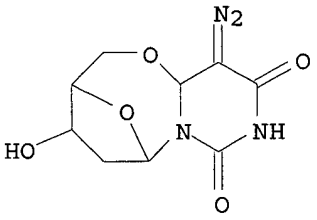
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4092305		19780530
APPLICATION INFO.:	US 1975-623909		19751020 (5)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1972-282362, filed on 6 Nov 1972, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Warren, Charles F.		
LEGAL REPRESENTATIVE:	Trask & Britt		
NUMBER OF CLAIMS:	16		

EXEMPLARY CLAIM: 1,10
LINE COUNT: 330
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB 5-ALKYL TRIAZENO URACIL COMPOUNDS AND DERIVATIVES THEREOF WERE SYNTHESIZED BY REACTING AN ALKYL AMINE SUCH AS DIMETHYLAMINE WITH A METHONAL ADDUCT OF 5-DIAZOURACIL AND NUCLEOSIDES THEREOF, UNDER STRINGENT REACTION CONDITIONS TO YIELD THE DESIRED COMPOUNDS. These alkyl triazeno uracil compounds have the structure ##STR1## wherein R is hydrogen or a carbohydrate group, particularly a pentose or hexose monosaccaride such as ribose, arabinose, glucose, and the like, and R' and R" are lower alkyl groups having one to four carbon atoms and wherein R' and R" may be the same or different alkyl groups. The compounds of this invention have been found especially effective as antibacterial and antifungal agents and in inhibiting carcinoma growth in animal tissue.

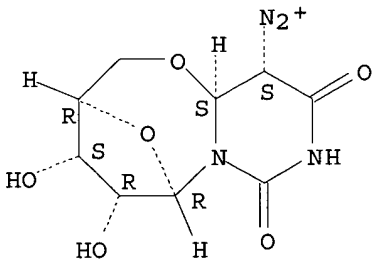
IT **67814-29-3 67971-95-3**
(reaction of, with dimethylamine)

RN 67814-29-3 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-8,10(9H)-dione, 11-diazo-3,4,5,6,11,11a-hexahydro-4-hydroxy- (9CI) (CA INDEX NAME)



RN 67971-95-3 USPATFULL
CN 3,6-Epoxy-2H,8H-pyrimido[6,1-b][1,3]oxazocine-11-diazonium, 3,4,5,6,9,10,11,11a-octahydro-4,5-dihydroxy-8,10-dioxo-, [3R-(3α,4α,5α,6α,11α,11aα)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 62 OF 84 USPATFULL on STN
ACCESSION NUMBER: 76:50624 USPATFULL
TITLE: Fused quinazolinones and a process for production thereof
INVENTOR(S): Inaba, Shigeho, Takarazuka, Japan
Yamamoto, Michihiro, Toyonaka, Japan
Ishizumi, Kikuo, Ikeda, Japan

Mori, Kazuo, Kobe, Japan
Koshiba, Masao, Takarazuka, Japan
Yamamoto, Hisao, Nishinomiya, Japan
PATENT ASSIGNEE(S): Sumitomo Chemical Company, Limited, Osaka, Japan
(non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 3980645		19760914
APPLICATION INFO.:	US 1974-521768		19741107 (5)

RELATED APPLN. INFO.: Division of Ser. No. US 1973-381571, filed on 23 Jul 1973, now patented, Pat. No. US 3891638 which is a continuation-in-part of Ser. No. US 1971-172562, filed on 17 Aug 1971, now abandoned

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1970-75817	19700827
	JP 1970-81593	19700916

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Thomas, Jr., James O.
ASSISTANT EXAMINER: Robinson, D. W.
LEGAL REPRESENTATIVE: Stevens, Davis, Miller & Mosher
NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1
LINE COUNT: 551
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

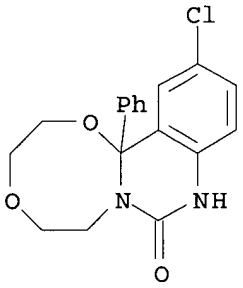
AB Fused quinazolinone derivatives of the formula, ##SPC1##

Wherein R.sub.1 and R.sub.2 are individually hydrogen, C.sub.1.sub.-4 alkyl, C.sub.1.sub.-4 alkoxy, nitro, C.sub.1.sub.-4 alkylsulfonyl or halogen; R.sub.3 is pyridyl, thienyl or a group of the formula ##SPC2##

Wherein R.sub. 4 is hydrogen or halogen; R is hydrogen, C.sub.1.sub.-4 alkyl, C.sub.2.sub.-5 alkenyl, aralkyl, (C.sub.3.sub.-6 cycloalkyl)C.sub.1.sub.-4 alkyl, (C.sub.1.sub.-4 alkoxy)C.sub.1.sub.-4 alkyl, (C.sub.1.sub.-4 alkylthio)C.sub.1.sub.-4 alkyl, hydroxy-C.sub.1.sub.-4 alkyl or C.sub.2.sub.-5 alkanoyloxy-C.sub.1.sub.-4 alkyl; Y is oxygen, or a group of the formula N - R.sub.5, wherein R.sub.5 is hydrogen or C.sub.1.sub.-4 alkyl; and Z is C.sub.2.sub.-5 alkylene or alkenylene, are prepared by reacting a trihaloacetamidophenyl ketone derivative of the formula, ##SPC3##

Wherein R.sub.1, R.sub.2, R.sub. 3 and R are as defined above; and X.sub.1, X.sub.2 and X.sub.3 are halogen, with an amine of the formula, HY - Z - NH.sub.2, wherein Y and Z are as defined above, or a salt thereof, in the presence of a solvent or a mixture thereof. They have remarkable pharmacological properties such as anti-inflammatory, analgesic and/or uricosuric activities.

IT **36105-75-6P**
(preparation of)
RN 36105-75-6 USPATFULL
CN 8H-[1,6,3]Dioxazocino[3,2-c]quinazolin-8-one, 12-chloro-2,3,5,6,9,13b-hexahydro-13b-phenyl- (9CI) (CA INDEX NAME)



L89 ANSWER 63 OF 84 USPATFULL on STN
ACCESSION NUMBER: 75:33337 USPATFULL
TITLE: Fused quinazolinones
INVENTOR(S): Inaba, Shigeho, Takarazuka, Japan
Yamamoto, Michihiro, Toyonaka, Japan
Ishizumi, Kikuo, Ikeda, Japan
Mori, Kazuo, Kobe, Japan
Koshiba, Masao, Takarazuka, Japan
Yamamoto, Hisao, Nishinomiya, Japan
PATENT ASSIGNEE(S): Sumitomo Chemical Co., Ltd., Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 3891638		19750624
APPLICATION INFO.:	US 1973-381571		19730723 (5)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1971-172562, filed on 17 Aug 1971, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Moatz, Harry I.
LEGAL REPRESENTATIVE: Stevens, Davis, Miller & Mosher
NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 1
LINE COUNT: 576
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Fused quinazolinone derivatives of the formula, ##SPC1##

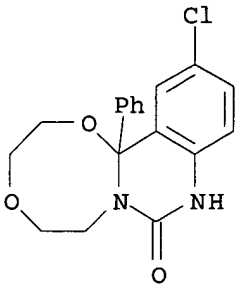
Wherein R.sub.1 and R.sub.2 are individually hydrogen, C.sub.1.sub.-4 alkyl, C.sub.1.sub.-4 alkoxy, nitro, C.sub.1.sub.-4 alkylsulfonyl or halogen; R.sub.3 is pyridyl, thienyl or a group of the formula ##SPC2##

Wherein R.sub.4 is hydrogen or halogen; R is hydrogen, C.sub.1.sub.-4 alkyl, C.sub.2.sub.-5 alkenyl, aralkyl, (C.sub.3.sub.-6 cycloalkyl)C.sub.1.sub.-4 alkyl, (C.sub.1.sub.-4 alkoxy)C.sub.1.sub.-4 alkyl, (C.sub.1.sub.-4 alkylthio)C.sub.1.sub.-4 alkyl, hydroxy-C.sub.1.sub.-4 alkyl or C.sub.2.sub.-5 alkanoyloxy-C.sub.1.sub.-4 alkyl; Y is oxygen, or a group of the formula N -- R.sub.5, wherein R.sub.5 is hydrogen or C.sub.1.sub.-4 alkyl; and Z is C.sub.2.sub.-5 alkylene or alkenylene, are prepared by contacting a trihaloacetamidophenyl ketone derivative of the formula, ##SPC3##

Wherein R.sub.1, R.sub.2, R.sub.3 and R are as defined above; and X.sub.1, X.sub.2 and X.sub.3 are halogen, with an amine of the formula, HY -- Z -- NH.sub.2, wherein Y and Z are as defined above, or a salt thereof, in the presence of a solvent or a mixture thereof. They have

remarkable pharmacological properties such as anti-inflammatory, analgesic and/or uricosuric activities.

IT **36105-75-6P**
(preparation of)
RN 36105-75-6 USPATFULL
CN 8H-[1,6,3]Dioxazocino[3,2-c]quinazolin-8-one, 12-chloro-2,3,5,6,9,13b-hexahydro-13b-phenyl- (9CI) (CA INDEX NAME)



L89 ANSWER 64 OF 84 USPATFULL on STN

ACCESSION NUMBER:	74:24998 USPATFULL
TITLE:	URICOSURIC AGENT
INVENTOR(S):	Yamamoto, Michihiro, Toyonaki, Japan Aono, Shunji, Toyonaki, Japan Nakatani, Hiroshi, Toyonaki, Japan Morooka, Shigeaki, Takarazuka, Japan Koshiba, Masao, Takarazuka, Japan Inaha, Shigeho, Takarazuka, Japan Aisaka, Akira, Minoo, Japan Yamamoto, Hisao, Nishinomiya, Japan
PATENT ASSIGNEE(S):	Sumitomo Chemical Company, Limited, Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 3812257		19740521	
APPLICATION INFO.:	US 1972-242215		19720407	(5)
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Friedman, Stanley J.			
LEGAL REPRESENTATIVE:	Stevens, Richard K.			
NUMBER OF CLAIMS:	20			
LINE COUNT:	480			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Excretion of uric acid from the body can be promoted by administering an effective amount of a quinazoline derivative represented by the formula ##SPC1##

Wherein R is a hydrogen atom, a lower alkyl group, a lower alkenyl group, an aralkyl group, a cycloalkyl group, a lower cycloalkylalkyl group, a lower alkoxyalkyl group, a lower alkanoyloxyalkyl group, a lower alkylthioalkyl group or a group of the formula -C.sub.n H.sub.2n -B (wherein n is zero or an integer of 1 to 3; B is a saturated or unsaturaged heterocyclic ring which may contain one or two hetero atoms selected from the group consisting of nitrogen, oxygen and sulfur) R.sub.1 and R.sub.2 are individually a hydrogen atom, a lower alkyl group, a lower alkoxy group, a trifluoromethyl group, a nitro group, a

lower alkylthio group, a lower alkylsulfonyl group or a halogen atom; Z is an oxygen atom or a sulfur atom; and A is a group of the formula, ##SPC2##

Wherein R.sub.3 is a phenyl group, a substituted phenyl group, a cycloalkyl group, a pyridyl group, a pyrrolyl group, a furyl group or a thienyl group; R.sub.4 and R.sub.5 are individually a hydrogen atom, a lower alkyl group, a lower alkenyl group, an aralkyl group, a cycloalkyl group, a lower cycloalkylalkyl group, a lower hydroxyalkyl group, a lower alkanoyloxyalkyl group, a lower alkoxyalkyl group, a lower alkylthioalkyl group, a phenyl group, a substituted phenyl group or a group of the formula ##SPC3##

(wherein n is an integer of 1 to 3; R.sub.7 and R.sub.8 are individually the same or different lower alkyl group, provided that R.sub.7 and R.sub.8 may form together with the adjacent nitrogen atom a five- or six-membered heterocyclic ring, which may further contain another nitrogen or oxygen atom); Y is an oxygen atom or a group of the formula ##SPC4##

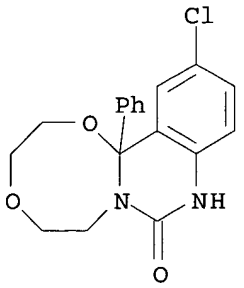
(wherein R.sub.9 is a hydrogen atom or a lower alkyl group); R.sub.6 is a lower alkyl group, a lower alkenyl group, an aralkyl group, a cycloalkyl group, a lower cycloalkylalkyl group, a lower hydroxyalkyl group, a lower alkanoyloxyalkyl group, a lower alkoxyalkyl group, a lower alkylthioalkyl group, a phenyl group, a substituted phenyl group or a group of the formula ##SPC5##

(wherein n is an integer of 1 to 3; R.sub.7 and R.sub.8 are individually the same or different lower alkyl group, provided that R.sub.7 and R.sub.8 may form together with the adjacent nitrogen atom a five- or six-membered heterocyclic ring, which may further contain another nitrogen or oxygen atom); moreover R.sub.5 and R.sub.6 may form a five- to eight-membered heterocyclic ring together with the adjacent Y and nitrogen atom and the carbon atom attached to both of them, and said heterocyclic ring may contain another nitrogen or oxygen atom, and further it may be optionally substituted by one or two lower alkyl groups, which may be joined to form a benzene or cyclohexane ring, or the non-toxic salts thereof.

IT **36105-75-6**
(uricosuric agent)

RN 36105-75-6 USPATFULL

CN 8H-[1,6,3]Dioxazocino[3,2-c]quinazolin-8-one, 12-chloro-2,3,5,6,9,13b-hexahydro-13b-phenyl- (9CI) (CA INDEX NAME)



=> d iall abeq tech abex 55-64

YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, TOXCENTER, USPATFULL, WPIX, BIOSIS, CANCERLIT, BIOTECHNO, BIOTECHDS, SCISEARCH' - CONTINUE? (Y)/N:y

'ABEQ' IS NOT A VALID FORMAT
'TECH' IS NOT A VALID FORMAT
'ABEX' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid in at least one of the files. Refer to file specific help messages or the STNGUIDE file for information on formats available in individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):end

=> d iall abeq tech abex 65-69
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, TOXCENTER, USPATFULL, WPIX, BIOSIS, CANCERLIT, BIOTECHNO, BIOTECHDS, SCISEARCH' - CONTINUE? (Y)/N:y

L89 ANSWER 65 OF 84 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN DUPLICATE 4
ACCESSION NUMBER: 2002-557536 [59] WPIX
DOC. NO. CPI: C2002-158226
TITLE: Producing a polypeptide polymer by self-assembly for use in lubricants and coating compositions, comprises polymerizing polypeptides capable of self-assembly in the presence of a divalent cation and template molecule.
DERWENT CLASS: B04 B07 D16
INVENTOR(S): BARTON, N; CHOW, K; LAFFERTY, W M; MATHUR, E J; SHORT, J
PATENT ASSIGNEE(S): (DIVE-N) DIVERSA CORP; (BART-I) BARTON N; (CHOW-I) CHOW K; (LAFF-I) LAFFERTY W M; (MATH-I) MATHUR E J; (SHOR-I) SHORT J
COUNTRY COUNT: 99
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2002044336	A2	20020606	(200259)*		182	C12N000-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW						
AU 2002027064	A	20020611	(200264)			C12N000-00
EP 1347770	A2	20031001	(200365)	EN		A61K038-00
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR						
US 2003198681	A1	20031023	(200370)			A61K039-395
JP 2004523219	W	20040805	(200451)		295	C12N015-09

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002044336	A2	WO 2001-US45001	20011130
AU 2002027064	A	AU 2002-27064	20011130
EP 1347770	A2	EP 2001-996025	20011130
		WO 2001-US45001	20011130
US 2003198681	A1 Provisional	US 2000-250426P	20001130
		US 2001-997807	20011130

JP 2004523219	W	WO 2001-US45001	20011130
		JP 2002-546685	20011130

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002027064	A Based on	WO 2002044336
EP 1347770	A2 Based on	WO 2002044336
JP 2004523219	W Based on	WO 2002044336

PRIORITY APPLN. INFO: US 2000-250426P 20001130; US 2001-997807 20011130

INT. PATENT CLASSIF.:

MAIN: A61K038-00; A61K039-395; C12N000-00; C12N015-09

SECONDARY: A61K009-16; A61K009-50; A61K009-51; A61K047-42; C07H021-04; C07K001-00; C07K001-02; C07K001-13; C07K001-14; C07K014-00; C07K014-47; C07K016-00; C07K016-18; C07K017-00; C07K019-00; C12N001-15; C12N001-19; C12N001-21; C12N005-10; C12N015-00; C12N015-19; C12P021-02; G01N033-53; G01N033-566; G01N037-00

BASIC ABSTRACT:

WO 200244336 A UPAB: 20021031

NOVELTY - Producing (M1) a polypeptide polymer (I) by self-assembly, involves providing a number of polypeptides capable of self-assembly in the presence of a divalent cation, and polymerizing the polypeptides in the presence of a divalent cation and a template molecule.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a drug delivery system (II), comprising a polymeric encapsulation medium (EM) made by self-assembly of a number of polypeptides, and a drug encapsulated in EM;

(2) encapsulating a molecule, by providing a solution of a number of polypeptides (III) comprising:

(i) a sequence (S1) of 207, 170, 178, 130 or 124 amino acids, given in the specification;

(ii) sequences having 50 % homology to S1, as determined by analysis with a sequences comparison algorithm or by visual inspection; and

(iii) polymerizing the polypeptides in the presence of the molecule so as to encapsulate the molecule in the polymer;

(3) encapsulating a molecule, by providing a solution of polypeptides encoded by a nucleic acid (IV) comprising:

(i) a sequence (S2) of 624, 513, 537, 311 or 372 base pairs (bp), given in the specification;

(ii) variants having 50 % homology to S2 over a region of 100 residues, as determined by analysis with a sequence comparison algorithm or by visual inspection;

(iii) sequences complementary to S2 or sequences complementary to variants having 50 % homology to S2 over a region of 100 residues; and

(iv) isolated nucleic acids that hybridize to nucleic acids having any of the above said sequences under conditions of low, moderate and high stringency, and polymerizing the polypeptides in the presence of the molecule so as to encapsulate the molecule in the polymer;

(4) generating a variant;

(5) assay for identifying functional polypeptide fragments or variants encoded by fragments of (IV);

(6) a polypeptide (IIIa) comprising:

(i) S1;

(ii) sequences having 50 % homology to S1, as determined by analysis

with a sequence comparison algorithm or by visual inspection; or

(iii) sequences encoded by (IV), and a functional group selected from an antibody, oligosaccharide, polynucleotide and polyethylene glycol;

(7) a nucleic acid probe (V) comprising an oligonucleotide of 10 - 50 nucleotides in length and having a segment of 10 contiguous nucleotides having 50 % complementary to a nucleic acid target region of S2, and which hybridizes to the nucleic acid target region under moderate to highly stringent conditions to form a detectable target:probe duplex;

(8) a separation agent, fiber, lubricant, coating composition, biochip, nanomechanical component, optical switch or an optical wave guide, comprising a polymer made by self-assembly of a number of polypeptides having 50 % homology to a polypeptide comprising S1;

(9) a computer readable medium (RM) having (IV) stored on it;

(10) a computer system (CS) comprising a processor and a data storage device having (IV) stored on it;

(11) a protein preparation comprising (III);

(12) an expression vector (VI) capable of replicating in a host cell comprising (IV); and

(13) a host cell comprising (VI).

USE - (I) is useful for delivering a drug to a location in the human or animal body. Polypeptides (III) are useful for encapsulating a molecule. The polymeric separation agent is useful for isolating a **chiral** compound from a mixture. A nucleic acid (IV) is useful for comparing a first sequence to a second sequence, where the first sequence is (IV), and for identifying a feature in a particular sequence (claimed). (III) is useful in fibers, polymeric separation agent, coating compositions, biochips, nanomechanical components, optical switches and optical wave guides.

Dwg.0/4

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B04-B03C; B04-C01G; B04-C02X; B04-C03; **B04-C03C**; B04-E01; B04-E05; B04-E08; B04-F0100E; B04-G01; B04-N04; B04-N0400E; B04-N08; B11-C08; B11-C08D2; B11-C08E3; B11-C08E4; B11-C08E5; B11-C08E6; B12-K04; B12-K04F; B12-M11E; D05-C12; D05-H09; D05-H10; D05-H12D1; D05-H12E; D05-H14; D05-H17A; D05-H17C; D05-H17C1

TECH UPTX: 20020916

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Polypeptide: (II) further comprises a targeting vector. (III) has 50 %, preferably 90 %, homology to S1 or 10 consecutive amino acids of S1. (III) is encoded by (IV). Variants of (IV) have about 50 %, preferably 90 %, homology to S2 over a region of about 200 residues. (III) further comprises a functional group comprising a polynucleotide, polyethylene glycol, oligosaccharide or antibody. Preferred Method: M1 further involves providing a number of polypeptides, by:

(a) preparing a vector with a nucleic acid attached, where the nucleic acid encodes the polypeptide;

(b) inserting the vector into a host cell;

(c) growing the host cell in a suitable culture to express the nucleic acid to form the polypeptide; and

(d) isolating the formed polypeptide from the host cell.

The method further involves dissolving the polypeptides in a solution, and adding a template molecule and alkaline earth metal ions to the solution. The vector comprises plasmid pEX-CAN-A. The host cell comprises Escherichia coli BL21 (DE3) or Pseudomonas. Preferred System: CS further comprising a sequence comparison algorithm and a data storage device having a reference sequence stored on it. The sequence comparison algorithm comprises a computer program which indicates polymorphisms. The

system further comprises an identifier which identifies one or more features in the sequence. The differences between first sequence and second sequence is determined by identifying polymorphisms.

ABEX UPTX: 20020916

WIDER DISCLOSURE - The following are disclosed:
(1) shuffling, assembling, reassembling, recombining and/or concatenating two polynucleotides;
(2) a non-stochastic method termed synthetic ligation reassembly (SLR);
(3) random, pseudorandom and defined sequence framework peptide libraries, and methods for generating and screening the libraries;
(4) shuffling a pool of polynucleotides;
(5) peptide libraries comprising a number of individual library members;
(6) a product-by-process for selecting polynucleotide sequences having a predetermined binding specificity;
(7) selecting a subset of polynucleotides from a starting set of polynucleotides; and
(8) producing a heat stable enzyme.

SPECIFIC SEQUENCES - (III) comprises a sequence of 207, 170, 178, 130 or 124 amino acids fully defined in the specification, and (IV) comprises a sequence of 624, 513, 537, 311 or 372 nucleotides fully defined in the specification (claimed).

EXAMPLE - Vector pET17b was linearized with NdeI and NotI and dephosphorylated with CIP. Then the NdeI and NotI sites were attached to the **genes** to be **expressed** by polymerase chain reaction (PCR). The formed PCR products were cleaved with NdeI and NotI, separated on an agarose gel and isolated. The obtained fragments were ligated and transformed in DH5alpha cells. The transformants were checked for their insert size. The resulting plasmid such as pEX-CAN-A was prepared from suitable transformants, and for the control, the transition sites from the vector to the insert were sequenced. 250 g frozen cell mass of recombinant Escherichia coli were suspended in 600 ml buffer, and lysed. The viscosity of the solution was lowered by shearing the DNA and by adding additional 400 ml buffer. Particles were centrifuged and a clear supernatant (crude extract) was obtained. To precipitate the heat-sensitive protein, the crude extract was heated to 100 degrees Centigrade. The heat-treated crude extract was centrifuged. The dialyzed protein solution was diluted by addition of buffer to a final protein concentration of 6.5 mg/ml. The diluted protein solution was rapidly heated to 80 degrees Centigrade and then immediately transferred into a 500 ml screw-capped storage bottle. The storage bottle contained 3.32 ml (21.58 mg protein) of Polymer Primers. CaCl and MgCl were added to the mixture and the closed bottle was stored at 60 degrees Centigrade. After addition of the salts, the solution became immediately turbid, indicating rapid polymerization of protein units. After 10 minute polymerization, the formed Polymer fibers were sheared to create additional polymer primers to speed up polymerization. Polymer or polymer fibers were observed under an electron microscope. After 1 - 2 hours of polymerization, protein polymers were completely removed from the solution by centrifugation. Yield of polymer: 2.1 grams (protein) from 250 grams (wet weight) of E. coli (about 1 g Polymer (dry weight)/119 g E. coli.

L89 ANSWER 66 OF 84 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-203534 [19] WPIX
DOC. NO. CPI: C2004-080212
TITLE: Novel single or multiple target oligonucleotide anti-sense to e.g. initiation codons and introns of respiratory disease-relevant genes e.g., CCR1, RANTES, MCP4, useful for prophylaxis or treating respiratory

disease e.g., asthma.
DERWENT CLASS: A89 A96 B04 D16
INVENTOR(S): AGUILAR, D; CONG, H; LU, H; MILLER, S; NYCE, J W; SANDRASAGRA, A; SHAHABUDDIN, S; TANG, L
PATENT ASSIGNEE(S): (EPIG-N) EPIGENESIS PHARM INC
COUNTRY COUNT: 105
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004011613	A2	20040205	(200419)*	EN	85	C12N000-00
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW						
AU 2003268032	A1	20040216	(200453)			C12N000-00

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004011613	A2	WO 2003-US23509	20030725
AU 2003268032	A1	AU 2003-268032	20030725

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003268032	A1 Based on	WO 2004011613

PRIORITY APPLN. INFO: US 2002-399076P 20020729
INT. PATENT CLASSIF.:
MAIN: C12N000-00
BASIC ABSTRACT:
WO2004011613 A UPAB: 20040318
NOVELTY - An oligonucleotide (oligo) (I) anti-sense to e.g., initiation codon, coding region with 2-10 nucleotides of 5'-end and 3'-end of nucleic acid target comprising gene(s) chosen from e.g. interleukin (IL)-4 receptor, IL-5 receptor or salts of (I) and optionally surfactant operatively linked to (I), is new.

DETAILED DESCRIPTION - An oligonucleotide (oligo) (I) that is anti-sense to an initiation codon, a coding region, a 5', or 3' intron-exon junction, an intron, a region with 2-10 nucleotides of the 5'-end and the 3'-end or a border section between a coding and non-coding region of a nucleic acid target comprising a gene(s) chosen from interleukin-4 receptor, interleukin-5 receptor, CCR1, CCR3, Eotaxin-1,RANTES, MCP4, CD23, ICAM, VCAM, tryptase a, tryptase b, PDE4 A, PDE4 C or PDE4 D gene, or anti-sense to their corresponding mRNAs, or salts of (I), and optionally a surfactant that may be operatively linked to (I).

INDEPENDENT CLAIMS are included for:

(1) a composition (II) comprising (I) and carrier or diluent and optionally therapeutic agent;

(2) a formulation (III) comprising (II), the carrier comprises a hydrophobic carrier;

(3) a capsule or cartridge (IV), comprising (III);

(4) a vector (V), comprising (I);

(5) a cell (VI) comprising (I);

(6) a diagnostic or therapeutic kit (VII) for delivery of an oligonucleotide(s) comprising, in separate containers, a delivery device, (II) and instructions for loading (III) into the device and for its use; and

(7) screening (M1) a candidate compound for the prevention and/or treatment of a respiratory or lung disease that binds to one or more nucleic acid target(s) or **expressed** product(s) comprising a **gene**(s) chosen from above mentioned genes.

ACTIVITY - Antiinflammatory; Antiasthmatic; Antiallergic; Hypotensive.

MECHANISM OF ACTION - Antisense therapy.

Eosinophils are predominant effector cells in allergic diseases, which were attracted by several CC chemokines into the inflammatory tissue. The human eosinophils are recruited by eotaxin, RANTES and MCP-3 and MCP-4 through CCR3. These chemokines were potential therapeutic target for asthma and other allergic diseases. The effect of antisense oligonucleotides (ASODNs) (17-20 bases in length) designed to hybridize to the specific sequence in the 3'- and 5'-untranslated regions as well as the coding regions of RANTES and MCP-4 mRNA, in the inhibition of mRNA and protein expression in BEAS-2B human airway epithelial cells was studied as follows. Confluent monolayers of BEAS-2B cells were either treated with culture medium, or transfected with RANTES specific antisense e.g., ATTTTTCATGTTTGCCAGTA, GAGTGCAGTGTTCCTTCCTCCCTT, CAGTGTTCCTCCCTTCTTTG, TTCCTCCCTTCCTTGCCTCT, CCCTTCCTTGCCTCTAGAGG, CCTTGCCTCTAGAGGCATGC, or MCP-4 specific antisense e.g., TCTGGCTGAGCAAGTCCCTG, TGCATTCATCTTTCCACAAT, AGAGCTCTCCTTCCTACATT, TTCCTACATTGCGGCATCCC, ACATTGCGGCATCCCTTCAT or Wobble, a control ASODN (5 mu g/ml), in the presence of lipofectin (10 micro g/ml), a carrier lipid, for 4 hours followed by a 4 hours (for mRNA expression) or 18 hours (for protein expression) treatment with the complete medium. mRNA expression was determined by TaqMan using a specific MCP-4 or RANTES probe. 43% of ASODNs specific to MCP-4 and 32% of RANTES ASODNs showed more than 50% inhibition of MCP-4 and RANTES mRNA expression respectively. The level of MCP-4 or RANTES protein in the conditioned medium of the BEEAS-2B cells, either untransfected with specific or control ASODNs was determined by enzyme linked immunosorbent assay (ELISA). The results showed undetectable levels of MCP-4 and low levels of RANTES expression in BEAS-2B cells treated with medium only. Treatment of BEAS-2B cells with TNF alpha and IFN gamma induced the levels of both chemokines. Treatment of BEAS-2B cells with antisense prior to cytokine treatment, inhibited protein expression. 8% of MCP-4 ASODNs and 15% of RANTES ASODNs inhibited greater than 25% and 50% of MCP-4 and RANTES protein expression respectively. These findings suggested that ASODNs can inhibit RANTES and MCP-4 expression.

USE - (I) is useful for reducing or inhibiting **expression** of a **gene** or mRNA encoding interleukin-4 receptor, interleukin-5 receptor, CCR1, CCR3, Eotaxin-1, RANTES, MCP4, CD23, ICAM, VCAM, tryptase a, tryptase b, PDE4 A, PDE4 B, PDE4 C, or PDE4 D, which involves contacting (I) with cells or tissues, under conditions effective for hybridization, and allowing hybridization to occur, whereby expression is reduced or inhibited. The hybridization is conducted under stringent condition or semi-stringent condition, in vitro. The hybridization is conducted under physiological condition in vivo. (II) is useful for preventing or treating a respiratory or lung disease, which involves administering to the airways of a subject an effective amount of an inhibitor of one or more nucleic acid target(s) or expressed product(s), preferably inhibitor is (II), comprising a gene(s) chosen from above mentioned genes. (II) comprises solid powdered or liquid particles of about 0.5-10 micro in size of about 10 micro to about 500 micro in size. (II) further comprises other therapeutic agents. The therapeutic agent(s)

comprise(s) anti-adenosine A1, A2b or A3 receptor agents or adenosine A2a receptor stimulating agents other than the nucleic acid(s). () further comprising administering a surfactant. The surfactant comprises lipid or non-lipid surfactant. The respiratory or lung disease is associated with hyperresponsiveness to and/or increased levels of, adenosine and/or levels of adenosine (A) receptor(s), and/or asthma and/or lung allergy(ies) associated with inflammation or an inflammatory disease. The subject is a mammal. The mammal is a human or a non-human mammal. The oligo is obtained by selecting fragments of a target nucleic acid having 4 or more contiguous bases consisting of G or C, and obtaining a second oligo 4-60 nucleotides long comprising a sequence that is anti-sense to the selected fragment. The inhibitor is chosen from dansylcadaverin, glycinamide, methylamine, n-propylamine, n-hexylamine, bacitracin, ethylamine, t-butylamine, an antibody to the expressed product or (I) or its combination. The method further involves administering a subject of interest with one or more anti-asthma agent(s). The oligo is anti-sense to two or more **genes**, **expressed** sequence tags (ESTs) or RNAs. (I) is useful for production of a medicament for the prevention and/or treatment of a respiratory or lung disease. The respiratory or lung disease is chosen from airway inflammation, allergy(ies), asthma, impeded respiration, cystic fibrosis (CF), chronic obstructive pulmonary diseases (COPD), allergic rhinitis (AR), acute respiratory distress syndrome (ARDS), pulmonary hypertension, lung inflammation, bronchitis, airway obstruction (claimed).

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: A12-V01; A12-V03C2; A12-W11L; B01-D02; B04-B03C; B04-C03; **B04-C03C**; B04-E01; B04-E05; B04-E06; B04-E08; B04-F0100E; B04-G01; B04-L01; B05-B01M; B05-B01P; B05-B02A; B07-D09; B07-D13; B07-F01; B10-A08; B10-A22; B10-B04B; B10-C04E; B10-D03; B10-E02; B10-E04B; B10-E04C; B10-F01; B11-C; B11-C03; B11-C04; B11-C06; B11-C08E; B11-C08F; B12-K04; B12-M10; B12-M11G; B14-G02A; B14-K01; B14-N04; D05-C07; D05-H08; D05-H09; D05-H12D2; D05-H12D4; D05-H12E; D05-H14; D05-H18; D05-H19

TECH UPTX: 20040318

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Oligonucleotide: (I) is anti-sense to 2499 sequences e.g., CTC-CAC-TCA-CTC-CAG-GTG, CTC-CAC-TCA-CTC-CAG, GCA-GCT-GCC-CCA-TGC-TG, GAG-AAG-GCC-TTG-TAA-CC, GCG-CCC-CTG-CTC-CAT-TCG-CC, TTT-CTT-CCA-GCT-CTG-TGT, CAC-CAC-GCC-CGG-CTT-CTG-TGT, TCT-GCC-CGC-CTC-AGC-CTC-T, GGC-ACC-AGG-CTG-GTC-TCG, TGG-GAG-ATG-CCA-AGG-CAC, GCA-AAG-CCA-CCC-CAT-TGG, GTT-CCC-AGA-GCT-TGC-CAC-CT. (I) is anti-sense to two or more genes or RNAs. In (I), two or more mononucleotide is substituted or modified by one or more of phosphorothioate, **chiral** phosphorothioate, phosphorodithioate, phosphotriester, aminoalkylphosphotriester, methyl phosphonate, 3'-alkylene phosphonate, **chiral** phosphonate, phosphinate, phosphoramidate, 3'-amino phosphoramidate, aminoalkylphosphoramidate, thionophosphoramidate, thionoalkylphosphonate, thinoalkylphosphotriester, boranophosphate, alkene, sulfamate, methyleneimino, methylenehydrazino, sulfonate, sulfonamide, amide, thioether, carbonate, carbamate, sulfate, sulfite, hydroxylamine, methylene(methyimino), methyleneoxy (methylimino), 2'-O-methyl, or phosphoramidate residues, or its combinations, where all mononucleotides are preferably substituted or modified. In (I), one or more mononucleotide is substituted or modified at the 2' position by one or more of OH, F, O-, S-, N-alkyl, O-alkyl-O-alkyl N-alkenyl, N-alkynyl, O((CH2)n O)m CH3, O(CH2)n OCH3, O(CH2)2 ON(CH3)2, O(CH2)n NH2, O(CH2)n

ONH2, or O(CH2)n ON((CH2)n CH3))2, where n or m are from 1 to 10, C1 to C10 lower alkyl, substituted lower alkyl, alkaryl, aralkyl, O-alkaryl, O-aralkyl, SH, SCH3, OCN, Cl, Br, CN, CN3, OC3, SOCH3, SO2 CH3, ONO2, N3, NH2, heterocycloalkyl, heterocycloalkaryl, aminoalkylamino, poly-alkylamino, or substituted silyl. In (I), one or more mononucleotide is substituted or modified by one or more of 5-methylcytosine (mC), 5-hydroxymethyl cytosine, xanthine, hypoxanthine, 2-aminoadenine, 6-methyl adenine, 6-methyl guanine, 2-propyl adenine, 2-propyl guanine, 2-thiouracil, 2-thiothymine, 2-thiocytosine, 5-halouracil, 5-halocytosine, 5-propynyl uracil, 5-propynyl cytosine, 6-azo uracil, 6-azo cytosine, 6-azo thymine, 5-uracil (pseudouracil), 4-thiouracil adenine, 8-halo adenine, 8-amino adenine, 8-thiol adenine, 8-thioalkyl adenine, 8-hydroxyl adenine, 8-halo guanine, 8-amino guanine, 8-thiol guanine, 8-thioalkyl guanine, 8-hydroxyl guanine, 5-bromo uracil, 5-trifuloromethyl uracil, 5-bromo cytosine, 5-trifluoromethyl cytosine, 7-methylguanine, 7-methyladenine, 8-azaguanine, 8-azaadenine, 7-deazaguanine, 7-deazaadenine, 3-deazaguanine, 3-deazaadenine, 2-aminopropyladenine, 5-propylnyluracil, 5-propynylcytosine or 5-methylcytosine. The methylated cytosine (mC) is substituted for an unmethylated cytosine (C) in one or more CpG dinucleotide if present in (I). (I) contains adenosine (A), one or more A is substituted by a universal base chosen from heteroaromatic bases that bind to a thymidine base but having antagonist activity or less than about 0.3 of the adenosine base agonist activity at the adenosine A1, A2b or A3 receptors, or heteroaromatic bases that have no activity or have agonist activity at the adenosine A2a receptor. Substantially all A's are substituted by a universal base(s) chosen from heteroaromatic bases that bind to a thymidine base but either have antagonist activity or less than about 0.3 of the adenosine base agonist activity at the adenosine A1, A2b, or A3 receptors, or heteroaromatic bases that have no activity or have agonist activity at the adenosine A2a receptor. The heteroaromatic bases are chosen from pyrimidines or purines that may be substituted by O, halo, NH2, SH, SO, SO2, SO3 COOH, or branched or fused primary or secondary amino, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxy, alkenoxy, acyl, cycloacyl, arylacyl, alkynoxy, cycloalkoxy, aroyl, arylthio, arylsulfoxyl, halocycloalkyl, alkylcycloalyl, alkenylcycloalkyl, alkynylcycloalkyl, haloaryl, alkylaryl, alkenylaryl, alkynylaryl, arylalkyl, arylalkenyl, arylalkynyl, or arylcycloalkl, which may be further substituted by O, halo, NH2, primary, secondary or tertiary amine, SH, SO, SO2, SO3, cycloalkyl, heterocycloalkyl or heteroaryl. The pyrimidines are substituted at a 1, 2, 3, and/or 4 position, and the purines are substituted at a 1, 2, 3, 4, 7 and/or 8 position. The pyrimidines or purines are chosen from theophylline, caffeine, dyphylline, etophylline, piperazine, bamifylline, enprofylline or xanthine. The universal base is chosen from 3-nitropyrrole-2'-deoxynucleoside, 5-nitroindole, 2-deoxyribosyl-(5-nitroindole), 2-deoxyribofuranosyl-(5-nitroindole), 2'-deoxyinosine, 2'-deoxynebularine, 6H, 8H-3, 4-dihydropyrimido (4,5-c) oxazine-7-one or 2-amino-6-methoxyaminopurine. (I) consists of up to about 10% A, preferably 5% or 3% A (I) is more preferably free of A. The nucleic acid is linked to an agent that enhances cell internalization or up-take and/or a cell targeting agent. The cell internalization or up-take enhancing agent comprises transferring, asialoglycoprotein or streptavidin. The cell targeting agent comprises a vector, and the nucleic acid is operatively linked to the vector. The vector comprises a prokaryotic or eukaryotic vector.

Preferred Composition: In (II), the carrier or diluent comprises gaseous, liquid or solid carrier or diluent. The therapeutic agents comprise surfactants, antioxidants, flavoring and coloring agents, filler, volatile oils, buffering agents, dispersants, RNA inactivating agents, antioxidants, flavoring agents, propellants or preservatives. The

surfactants are lipid or non-lipid surfactants. The surfactants comprises surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D, surfactant protein E, its active fragments, non-dipalmitoyl disaturated phosphatidylcholine, dipalmitoylphosphatidylcholine, phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, phosphatidic acid, ubiquinones, lysophosphatidylethanolamine, lysophosphatidylcholine, palmitoyl-lysophosphatidylcholin, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycero-3-phosphocholine, dihydroxyacetone, palmitate, cytidine diphosphate (CDP) diacylglycerol, CDP choline, choline, choline phosphate, artificial lamellar bodies vehicles for surfactant components, omega-3 fatty acids, polyenic acid, polyenoic acid, lecithin, palmitic acid, non-ionic ethylene and/or propylene oxide block copolymers, polyoxypropylene, polyoxyethylene, poly(vinyl amine) with dextran and/or alkanoyl side chains, polyoxy ethylene 23 lauryl ether (Brij 35 (RTM)), t-octyl phenoxy polyethoxy ethanol (Triton X-100 (RTM)), depalmitoyl phosphatidyl choline (DPPC), phosphatidyl glycerol (PG) (ALEC (RTM)), tyloxapol (Exosurf (RTM)), surfactant-associated proteins (Survanta (RTM)) or C22H19C10 (Atovaquone (RTM)). The RNA inactivating agent comprises an enzyme. The enzyme is a ribozyme. (I) further comprises propellant. (I) is present in an amount of about 0.01 - 99.99 w/w of (II).

Preferred Formulation: (III) is chosen from intrabuccal, intrapulmonary, respirable, nasal, inhalable, intracavitary, intraorgan, or slow release formulations. The carrier is chosen from a solid or liquid carrier. (III) comprises a sprayable or aerosolizable powder, solution, suspension or emulsion, aqueous or alcoholic solution or oily solution or suspension, or oil-in-water or water-in-oil emulsion. (III) comprises a formulation of particle size about 0.5 microns to 10 microns, or 10 mu to about 500 microns. (III) preferably comprises a nasal formulation of particle size about 10 microns to about 500 microns. (III) is a respirable or inhalable formulation comprising a solid powdered or liquid aerosol or spray of particle size about 0.5 microns to about 10 microns. (III) is given in bulk or in single or multiple unit dose form.

Preferred Kit: In (VII) delivery device comprises a nebulizer, a dry powder inhaler, a pressurized inhaler or insufflator. The delivery device delivers single metered doses. The delivery device is adapted for receiving and piercing or opening a capsule(s), blister(s), or cartridge(s) and producing a solid powdered or liquid aerosol or spray. In (VII), (II) is in an inhalable, respirable, nasal, intracavitary, intraorgan or intrapulmonary formulation. (II) has particle size about 0.5-10 microns or preferably about 10-500 microns. (II) is provided in a pierceable or openable capsule, blister or cartridge. (III) comprises the delivery device, a surfactant, (II) and other therapeutic agents. (VII) further comprises a solvent chosen from organic solvents or organic solvents mixed with one or more co-solvents.

Preferred Method: In(M1), the nucleic acid target(s) or their expressed product(s) is (are) in a purified form from the expression system. The expressed product(s) is (are) expressed in or on the cell. The binding is detected by a label. The candidate compound suppresses the expression of one or more nucleic acid target(s). (M1) further involves step of contacting a candidate compound with or introducing into a cell expressing the one or more nucleic acid target(s) or their expressed product(s), and detecting the suppression, reduction or inhibition of their expression. The suppression, reduction or inhibition is detected by measuring the level of the **transcribed** mRNA of the **genes.** The cell comprises a construct comprising a nucleic acid target that is linked to a reported gene system in a cell.

ABEX UPTX: 20040318

ADMINISTRATION - (II) is administered intrapulmonary, intraorgan, intracavitarily, intrabuccally, intranasally, by inhalation or into the subject's respiratory system.
(II) is administered in an amount of 0.005-150, preferably, 0.01-75, more preferably 1-50 mg/kg body weight (claimed).

EXAMPLE - No relevant example is given.

L89 ANSWER 67 OF 84 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-519262 [55] WPIX
DOC. NO. CPI: C2002-146897
TITLE: New atropsiomers of asymmetric xanthine compounds useful as labels in various molecular biology applications for substrates e.g. nucleotide.
DERWENT CLASS: B02 B04 D16
INVENTOR(S): LEE, L G; ROSENBLUM, B B; TAING, M C; ROSEMBLUM, B B
PATENT ASSIGNEE(S): (PEKE) PE CORP NY; (APPL-N) APPLERA CORP
COUNTRY COUNT: 97
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2002036832	A2	20020510	(200255)*	EN	89	C12Q001-68
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW						
AU 2002030914	A	20020515	(200258)			C12Q001-68
US 6448407	B1	20020910	(200263)			C07D311-82
US 2003055243	A1	20030320	(200323)			C09B047-04
EP 1330550	A2	20030730	(200350)	EN		C12Q001-68
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR						
US 6649769	B2	20031118	(200376)			C07D403-04<--
JP 2004532805	W	20041028	(200471)		154	C07D311-82
US 2004229235	A1	20041118	(200477)			C12Q001-68

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2002036832	A2		WO 2001-US48654	20011030
AU 2002030914	A		AU 2002-30914	20011030
US 6448407	B1		US 2000-704966	20001101
US 2003055243	A1	Cont of	US 2000-704966	20001101
			US 2002-227058	20020821
EP 1330550	A2		EP 2001-991171	20011030
			WO 2001-US48654	20011030
US 6649769	B2	Div ex	US 2000-704966	20001101
			US 2002-227058	20020821
JP 2004532805	W		WO 2001-US48654	20011030
			JP 2002-539575	20011030
US 2004229235	A1	Div ex	US 2000-704966	20001101
		Div ex	US 2002-227058	20020821
			US 2003-716165	20031118

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002030914	A Based on	WO 2002036832
US 2003055243	A1 Cont of	US 6448407
EP 1330550	A2 Based on	WO 2002036832
US 6649769	B2 Div ex	US 6448407
JP 2004532805	W Based on	WO 2002036832
US 2004229235	A1 Div ex	US 6448407
	Div ex	US 6649769

PRIORITY APPLN. INFO: US 2000-704966 20001101; US
2002-227058 20020821; US
2003-716165 20031118

INT. PATENT CLASSIF.:
MAIN: C07D311-82; **C07D403-04**; C09B047-04; C12Q001-68
SECONDARY: C07D405-12; C07H019-04; C07H021-00; C07H021-04; C07K014-00; C09B011-04; C09B062-00; C09B067-00; C12N015-09; G01N033-533; G01N033-58

BASIC ABSTRACT:

WO 200236832 A UPAB: 20020829

NOVELTY - Atropisomer of asymmetric xanthine compounds (I) are new.

DETAILED DESCRIPTION - Atropisomer of xanthine compounds of formula (I) including aryl-substituted forms are new.

Z1 = OH, NH2, NHR or NR2;

R = H, 1-12C alkyl, phenyl, benzyl, aryl, heterocycle or a linking moiety;

Z2 = O, +NH2, +NHR or +NR2; and

X = carboxylate or sulfonate.

INDEPENDENT CLAIMS are also included for:

(1) an energy-transfer dye comprising a donor dye (a) capable of absorbing light at a first wavelength and emitting excitation energy in its response, an acceptor dye (b) capable of absorbing the excitation energy emitted by (a) and fluorescing at a second wavelength in response, and a linker (c) for linking (a) and (b). (a) and (b) are of formula (II). At least one of (a) and (b) is a pure atropisomer for xanthene compound;

(2) a labeled **nucleoside** or **nucleotide** of formula (III);

(3) a labeled **polynucleotide** (A') comprising **polynucleotide** covalently attached to a label (compound (I)) or a polypeptide covalently attached to (I);

(4) a phosphoramidite compound of formula R30-N(R31)-P(OR32)-O-L'-DYE (IV);

(5) formation of a labeled substrate involving reacting a substrate selected from **polynucleotide**, **nucleotide**, **nucleoside**, polypeptide, carbohydrate, ligand, enantiomerically pure compound, particle or surface with a linker (preferably N-hydroxysuccinimide or phosphoramidite) to form labeled substrate;

(6) synthesizing labeled **polynucleotide** involving coupling the phosphoramidite to **polynucleotide.** The **polynucleotide** is bound to a solid support;

(7) method (A) of separating atropisomers of 11C aminomethyl, 19C carboxyl fluorescein involving reacting 11C aminomethyl, 19C carboxyl fluorescein with an active ester or carboxylic acid to form diastereomeric carbamate, separating the diastereomeric carbamate and hydrolyzing the separated diastereomer with aqueous acid;

(8) method (B) of separating mixture of labeled substrate comprising (I) or energy-transfer dye involving separating a mixture of labeled substrates by electrophoresis or chromatography and detecting the labeled substrate by fluorescence detection;

(9) generating a labeled primer extension product involving extending

a primer-target hybrid with a **nucleotide**, where the primer or the **nucleotide** is labeled with (I) or energy-transfer compound;

(10) **polynucleotide** sequencing involving forming a mixture of first, second, third and a fourth class of **polynucleotides** and separating the **polynucleotide** on the basis of size. Each **polynucleotide** in the first class includes a 3'-terminal dideoxyadenosine and is labeled with a dye. Each **polynucleotide** in the second class includes a 3'-terminal dideoxycytidine and is labeled with a second dye. The **polynucleotide** in the third class includes a 3'-terminal dideoxyguanosine and is labeled with a third dye. The **polynucleotide** in the fourth class includes a 3'-terminal dideoxythymidine and is labeled with a fourth dye. At least one of first, second, third or fourth dye is compound (I) or the energy-transfer dye. The other dyes are spectrally resolvable from each other;

(11) **oligonucleotide** ligation involving annealing two probes to a target sequence and forming a phosphodiester bond between the 5' terminus of one probe and the 3' terminus of the other probe. At least one of the probe is labeled with (I) or the energy-transfer dye;

(12) fragment analysis involving separating labeled **polynucleotide** fragments by size-dependent separation process and detecting the separated-labeled **polynucleotide** fragments subsequent to the separation process. The fragments are labeled with (I) or energy-transfer dye;

(13) method of amplification involving annealing at least two primers to a target **polynucleotide** and extending the primers by polymerase and a mixture of **nucleotides.** At least one of the primers is a labeled **polynucleotide** (III) or (A');

(14) method of amplification involving annealing at least two primers and fluorescent dye-quencher probe to a target nucleic acid and extending the primers by polymerase and a mixture of **nucleotides**;

(15) a kit of labeling **polynucleotide** comprising compound including linking moiety or energy-transfer dye or phosphoramidite and a **polynucleotide**; and

(16) kit for generating labeled primer extension product comprising at least one **nucleotide** and a primer. The primer is labeled **polynucleotide.** At least one **nucleotide** is a labeled **nucleotide.**

Z', Z'2 = O, OH, NH2, NHR or NR2;

X' = X.

DYE = compound (I);

B = **nucleobase**;

L = linker;

R25 = H, monophosphate, diphosphate, triphosphate, thiophosphate or phosphate analog;

R26, R27 = H, HO, F or a moiety which blocks polymerase-mediated target-directed polymerization; or

R26+R27 = 2',3'-didehydroribose;

R30, R31 = 1-12C (cyclo)alkyl or aryl; or

NR30R31 = saturated nitrogen heterocycle;

R32 = phosphite ester protecting group;

L' = linker; and

n''' = 1-10.

USE - In molecular biology applications as labels for substances such as nucleotides, nucleoside, polynucleotide, polypeptide and carbohydrates and methods based on separation and detection of analytes. In methods utilizing fluorescent detection such as polymerase chain reaction amplification, DNA sequencing, antisense transcriptional and translational control of gene expression, genetic analysis and DNA probe-based diagnostic testing. For detecting differently labeled polynucleotides that have been subjected to biochemical separation procedure such as

electrophoresis. As labels for chiral substrates. As labels on 5'-labeled oligonucleotide primer for the polymerase chain reaction and other nucleic acid amplification and selection method.

ADVANTAGE - (I) Is substantially stable, pure and atropisomerically-enriched. (I) Exhibits beneficial effects for methods requiring simultaneous detection of multiple spatially-overlapping analytes. (I) prevents unwanted hindrance to analysis when used as a label for chiral substrate.

Dwg.0/15

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B04-B03A; B04-B03B; B04-C01; B04-C02; B04-E01; B04-E05; B05-B01J; B06-A03; B11-C07B3; B11-C08E4; B11-C08E5; B12-K04E; D05-H09; D05-H12; D05-H18B

TECH UPTX: 20020829

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: No general preparation given.

Preferred Compound: (I) is preferably of formula (I').

R1, R4, R5, R11, R13, R14 = T, T', 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-quinolyl, 3-quinolyl, 4-quinolyl, 2-imidazole, 4-imidazole, 3-pyrazole, 4-pyrazole, pyridazine, pyrimidine, pyrazine, cinnoline, pthalazine, quinazoline, quinoxaline, 3-(1,2,4-N)-triazolyl, 5-(1,2,4-N)-triazolyl, 5-tetrazolyl, 4-(1-O, 3-N)-oxazole, 5-(1-O, 3-N)-oxazole, 4-(1-S, 3-N)-thiazole, 5-(1S, 3-N)-thiazole, 2-benzoxazole, 2-benzothiazole, 4-(1,2,3-N)-benzotriazole or benzimidazole (preferably phenyl, naphthyl (both optionally substituted), F, Cl, 2-pyridyl, 3-pyridyl, 2-quinolyl, 3-quinolyl, methoxy or aminomethyl);

T = a linking moiety selected from azido, monosubstituted primary amine, disubstituted secondary amine, thiol, hydroxyl, halide, epoxide, N-hydroxysuccinimidyl ester, carboxyl, isothiocyanate, sulfonyl chloride, sulfonate ester, silyl halide, chlorotriazinyl, succinimidyl ester, pentafluorophenyl ester, maleimide, haloacetyl, epoxide, alkylhalide, allyl halide, aldehyde, ketone, acylazide, anhydride, iodoacetamide or an activated ester;

T' = F, Cl, 1-8C alkyl, carboxylate, sulfate, sulfonate, alkylsulfonate, aminomethyl (-CH2NH2), aminoalkyl, 4-dialkylaminopyridinium, hydroxymethyl (-CH2OH), methoxy (-OCH3), hydroxyalkyl (-ROH), thiomethyl (-CH2SH), thioalkyl (-RSH), alkylsulfone (-SO2R), arylthio (-SAr), arylsulfone (-SO2Ar), sulfonamide (-SO2NR2), alkylsulfoxide (-SOR), arylsulfoxide (-SOAr), amino, ammonium (-NH3+), amido (--CONR2), nitrile (-CN), 1-8C alkoxy (-OR), phenoxy, phenolic, tolyl, phenyl, aryl, benzyl, heterocycle, phosphonate, phosphate, quaternary amine, sulfate, polyethyleneoxy or linking moiety;

R13+R14 = benzo;

R17-R20 = T or T' (preferably Cl, F, 4-dialkylaminopyridinium, thiophenyl or thio-4-carboxyphenyl, especially Cl); and

Z1, Z2 = T;

provided that:

(i) when one of R18 and R19 is carboxyl or linking moiety then the other is H;

(ii) in (I'), when a first bridging group is taken together with Z1 nitrogen, the Z1-bonded carbon, and the R1-bonded C forms a 4-7 membered ring and optionally a second bridging group when taken together with Z2 nitrogen, the Z2-bonded C (optionally substituted by a linking moiety) and the R11-bonded C forms a second 4-7 membered ring;

(iii) at least one of the two rings has 5 members and contains one geminal disubstituted carbon (preferably 1-8C alkyl, especially methyl);

(iv) R1 or R11 is a linking moiety; and

(v) when R17 and R22 are Cl one of R18 and R19 is a linking group and the other H and X is carboxyl.

Preferred Dye: (a) Is (I) and (b) is (I), cyanine, phthalocyanine, squarane, bodipy, benzophenoxazine, fluorescein, dibenzorhodamine or rhodamine dye. (a) Is linked to (I), a polynucleotide (preferably 5'- or 3'-terminus of the polynucleotide) and a nucleobase of the polynucleotide. When the nucleobase is purine, (c) is attached at the 8-position, when the nucleobase is 7-deazapurine, (c) is attached at the 7- or 8-position and when the nucleobase is pyrimidine, (c) is attached at the 5-position.
Preferred Linker: (c) Is of formula -R21-Z-C(O)-, -R21-Z-C(O)-R22-R23-, DONOR-CH2-NH-C(O)-T''-NH-+C(O)-ACCEPTOR, DONOR-CH2-NH-C(O)-T''-CH2-NH-C(O)-ACCEPTOR, DONOR-CH2-NH-C(O)-T''-CH2-ACCEPTOR or D-CH2-NH-C(O)-T''-CH2-NH-(C(O)-T''-CH2NH)n'-C(O)-A (preferably -(CH2)n-NH-C(O)-).
Z = NH, S or O;
R21 = 1-12C alkyl attached to (a);
R22 = 1-12C alkylidinyl, 5-6 membered ring having at least one unsaturated bond or a fused ring attached to the carbonyl carbon (preferably cyclopentene, cyclohexene, cyclopentadiene, cyclohexadiene, furan, thiophene, pyrrole, isopyrrole, isoazole, pyrazole, isoimidazole, pyran, pyrone, benzene, pyridine, pyridazine, pyrimidine, pyrazine oxazine, indene, benzofuran, thionaphthalene, indole or naphthalene);
R23 = functional group that attaches (c) to (b) or -R24-Z-C(O)-;
n = 2-10;
R24 = 1-12C alkyl;
T'' = 1,4-phenylene;
D = donor dye;
A = acceptor dye; and
n' = 1-2.
Preferred Components: The labeled nucleotide or nucleoside is enzymatically incorporable or extendable and is a terminator. The labeled polynucleotide is of formula (IV) or (V).
R27 = H, OH, halide, azide, amine, alkylamine, 1-6C alkyl, allyl, 1-6C alkoxy, OCH3 or OCH2CH=CH2;
R28, R29 = H, phosphate, internucleotide phosphodiester or internucleotide analog;
X' = O, NH or S;
L = linker (preferably 1-12C alkydiyl, especially (CH2CH2O)n''); and
n'' = 1-100.
The polynucleotide comprises 2-100 nucleotides. The phosphoramidite compound is of formula N(CH3)2-P(OCH2CH2CN)-O-(CH2)6-NH-DYE. The substrate is enantiomerically pure. The fragments are labeled with mobility-modifying label.
Preferred Substrate: The enantiomerically pure compound is (+)-menthyl chloroformate or (-)-menthyl chloroformate. The labeled substrate comprises 11C aminomethyl, 19C-carboxyl fluorescein. The 19C-carboxyl fluorescein is 2-(4-aminomethyl-6-hydroxy-3-oxo-3H -xanthen-9-yl)-terephthalic acid. The particle is nanoparticle, microsphere, bead or liposome. The surface is glass. The active ester in (A) is menthyl chloroformate. The diastereomeric carbamate is separated by reverse-phase HPLC.
Preferred Process: The polynucleotide sequencing further includes detecting the separated polynucleotides by fluorescence detection and identifying the 3'-terminal nucleotide of the polynucleotide by the fluorescence spectrum of the dyes. The fragments are formed by ligation. The size dependent process is electrophoresis and the labeled polynucleotide fragments are detected by fluorescence.
Preferred Kit: The kit comprises four different terminators. One of which terminates at a target A, one terminates at target G, one terminates at target C and one terminates at target T or U.

ABEX UPTX: 20020829

SPECIFIC COMPOUNDS - 3 Compounds (I) are specifically claimed, e.g. 2,5-dichloro-3-(9-hydroxy-5-oxo-10- pyridin-3-yl-6,8-di-ortho-tolyl-5H-

benzo(a)xanthen-12-yl)-terephthalic acid (Ia).

EXAMPLE - 2-(4-((2-Isopropyl-5-methyl-cyclohexyloxycarbonylamino)-methyl)-3H-xanthen-9-yl)-terephthalic acid (1.1 g) was dissolved in water (100 ml) and cooled to 0 degrees C. Concentrated sulfuric acid (15 ml) was added drop wise to give a brownish solution. The temperature was allowed to rise to room temperature and the mixture was stirred overnight. The mixture was added to ice water (1.5 ml) and then adsorbed on pre-equilibrated C-18 silica gel. The support was washed with water until the pH of the eluant was neutral. The crude product was eluted with CH3OH (200 ml) which was concentrated under vacuum and dried to yield atropsiomer 2-(4-aminomethyl-3H-xanthen-9-yl)-terephthalic acid (0.93 g, 95 % yield) was obtained.

DEFINITIONS - Preferred Definitions:
Z1 = OH or NR2;
Z2 = O or N+R2;
X = carboxylate;
B = uracil, thymine, adenine, 7-deazaadenine, guanine or 7-deazaguanosine;
L = -C triple bond C-CH2-(OCH2CH2)n''-NH-C(O);
n'' = 0-2;
R30, R31 = isopropyl; or
NR30R31 = morpholino;
R32 = methyl, 2-cyanoethyl or 2-(4-nitrophenyl)ethyl;
L' = -(CH2CH2O)n'''-CH2CH2-NH-C(O)-); and
n''' = 1-10.

L89 ANSWER 68 OF 84 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-265893 [27] WPIX
DOC. NO. CPI: C2001-080452
TITLE: **Chiral** compound with poly(ether-thioether) backbone, useful as oligonucleotide analogs for e.g. therapeutic modulation of **gene expression**, hybridize with high sequence-specificity.
DERWENT CLASS: A25 A96 B04 D16
INVENTOR(S): SEGEV, D
PATENT ASSIGNEE(S): (BIRA) BIO-RAD LAB INC
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2001016365	A1	20010308	(200127)*	EN	119	C12Q001-68
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW						
AU 2000060126	A	20010326	(200137)			C12Q001-68
US 6348583	B1	20020219	(200221)			C07H019-00
EP 1208234	A1	20020529	(200243)	EN		C12Q001-68
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI						
JP 2003508062	W	20030304	(200319)		111	C12N015-09
AU 769619	B	20040129	(200412)			C12Q001-68

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001016365	A1	WO 2000-IL432	20000721
AU 2000060126	A	AU 2000-60126	20000721
US 6348583	B1 CIP of	US 1999-384995	19990820
		US 1999-411862	19991004
EP 1208234	A1	EP 2000-946256	20000721
		WO 2000-IL432	20000721
JP 2003508062	W	WO 2000-IL432	20000721
		JP 2001-520910	20000721
AU 769619	B	AU 2000-60126	20000721

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000060126	A Based on	WO 2001016365
EP 1208234	A1 Based on	WO 2001016365
JP 2003508062	W Based on	WO 2001016365
AU 769619	B Previous Publ.	AU 2000060126
	Based on	WO 2001016365

PRIORITY APPLN. INFO: US 1999-411862 19991004; US 1999-384995 19990830

INT. PATENT CLASSIF.:

MAIN: C07H019-00; C12N015-09; C12Q001-68

SECONDARY: A01N043-04; A01N061-00; A61K031-795; A61K048-00; A61P031-12; A61P035-00; A61P043-00; C07H021-00; C07H021-02; C07H021-04; C12N005-10

BASIC ABSTRACT:

WO 200116365 A UPAB: 20010518

NOVELTY - Compound (I) comprises a poly(ether-thioether/sulfone/sulfoxide) backbone that has many **chiral** carbon atoms and many ligands (II) individually linked to the **chiral** atoms. (II) include a naturally occurring nucleobase (NB) or an NB-binding group.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(a) intermediate compounds of formula (III);

(b) method for producing (I);

(c) sequence-specific hybridization process involving treatment of double-stranded nucleic acid with (I) so that (I) binds to one strand, causing displacement of the other strand;

(d) sequence-specific hybridization of (I) to a single-stranded nucleic acid; and

(e) pharmaceutical composition containing (I) as active ingredient, plus at least one of carrier, binder, thickener, diluent, buffer, preservative or surfactant.

B' = nucleobase or nucleobase-binding group;

X and Y = linkers;

Z = protecting group;

A = leaving group.

ACTIVITY - Antiviral; anti-inflammatory; antifungal; cytostatic; antipsoriatic; antibacterial; immunosuppressive; dermatological; fungicidal; anti-HIV; ophthalmological; antiasthmatic; cardiant; nephrotropic; gastrointestinal-gen.; osteopathic; antiarthritic; antirheumatic. No tests for the activity of (I) are given.

MECHANISM OF ACTION - Sequence-specific hybridization with DNA or RNA, in the same way as antisense oligonucleotides, also inhibition of nucleic acid degradation.

USE - (I) are used to form sequence-specific hybrids with single-stranded or double-stranded nucleic acid (in the second case,

causing displacement of one strand), particularly for modulating (inhibiting or activating) **gene expression** in vivo, by affecting **transcription**, **translation** or replication of the **gene.** They are used for treatment or prevention of essentially any disease where abnormal **gene expression** is involved, e.g. infections by viruses (including immune deficiency virus) or Candida albicans, cancer, inflammation, cardiovascular disorders, psoriasis, septic shock, warts, Kaposi's sarcoma, skin and systemic fungal infections, AIDS, pneumonia, flu, mononucleosis, retinitis and pneumonitis in immunosuppressed patients, asthma, cardiac infraction, kidney disease, gastrointestinal disease, osteoarthritis, rheumatoid arthritis, acute pancreatitis, Crohn's disease.

ADVANTAGE - (I) form hybrids with nucleic acid that are more stable than those formed with complementary DNA but not as stable as those formed with peptide nucleic acid. They are water soluble; stable against intra- or extra-cellular nucleases; can pass through cell walls; have low toxicity, and can be synthesized easily and efficiently.

Dwg.0/10

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: A12-V01; A12-W11L; **B04-C03C**; B04-E01; B04-E06; B05-B01B; B05-B01D; B05-B01M; B06-D09; B07-D12; B11-C08E4; B12-K04F; B14-A02; B14-A04; B14-C03; B14-C09; B14-E10; B14-F01; B14-F02; B14-G01B; B14-H01; B14-K01; B14-N03; B14-N10; B14-N13; B14-N17; B14-S06; D05-A02B; D05-H09; D05-H12; D05-H12D1; D05-H18A; D05-H18B

TECH UPTX: 20010518

TECHNOLOGY FOCUS - POLYMERS - Preferred materials: The **chiral** C atoms are separated by 4-6 intervening atoms and (I) particularly have formula (I').

(K), (I) = exoconjugate;

Q = sulfur, sulfoxide or sulfone;

The asterisk indicates a **chiral** C atom and the value of n is not specified. Especially, all XY is CH2CH2; (K) and (I) are poly(ethylene glycol) and at least 90-95, best over 99,% of the **chiral** C have (S) configuration.

Preparation: A monomer containing ether and thioether groups, and containing a **chiral** C atom attached to a functional group, is attached to a solid support. Further monomers are then coupled in a predetermined sequence, by standard chemical methods. The resulting polymers may then be oxidized, e.g. with m-chloroperbenzoic acid for sulfoxide and osmium tetroxide for sulfone.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Compounds: In (III), the nucleobase contains an amino group protected e.g. by benzamido or tert-butoxycarbonyl; Z is e.g. trityl or silyl; and A is e.g. halo, sulfonate, ammonium derivative or group replaceable by nucleophilic substitution.

Preparation: No general method for (III) is described but in examples preparation starts from methyl 4-hydroxycrotonate and involves (i) hydroxy protection; (ii) addition of mercaptoethanol; (iii) protection of hydroxy introduced in step (ii); (iv) ester reduction; (v) conversion of hydroxy produced in (iv) to methyl sulfonate ester; (vi) reaction with e.g. thymine; (vii) protection of 1-position of the thymine ring.

ABEX UPTX: 20010518

WIDER DISCLOSURE - (II) may also be a DNA interchelator or a reporter molecule, to produce compounds useful as probes in hybridization assays, polymerase chain reaction, sequencing etc.

ADMINISTRATION - (I) are administered e.g. topically, orally, by injection, optionally together with other antimicrobial or anti-inflammatory agents. No doses are suggested.
EXAMPLE - Controlled pore glass (CPG) derivatized with e.g. propylamine was reacted sequentially with succinic anhydride and 1-(dimethoxytrityl)hexaethylene glycol (in presence of condensing agents) to give a PEG(poly(ethylene glycol)-CPG conjugate. A sample of this (1 g) in a mixture of ethylene glycol dimethyl ether and potassium tert-butoxide in tetrahydrofuran, was treated with 3-(benzyloxymethyl)-1-(4-dimethoxytrityloxy-3-(2-(methylsulfonyloxy)ethylthio)but-1-yl)-thymine (Q; R/S mixture) (0.5 g). After reaction for 1 hour, solids were filtered off, washed and any unreacted hydroxy groups on the polymer capped by acetylation. The dimethoxytrityl groups were removed (trichloroacetic acid) and reaction with Q was repeated. The procedure was repeated as required, with the last cycle in the sequence being attachment of hexaethyleneglycol.

L89 ANSWER 69 OF 84 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 1998-467489 [40] WPIX
CROSS REFERENCE: 1997-435067 [40]; 1998-480786 [41]; 1998-506287 [43]; 1998-594477 [50]; 1998-594942 [50]; 1998-610387 [51]; 1999-034686 [03]; 1999-070058 [06]
DOC. NO. NON-CPI: N1998-364268
DOC. NO. CPI: C1998-141760
TITLE: Polyamide containing positive patch allowing for binding to minor groove of DNA - used for inhibiting **gene expression.**
DERWENT CLASS: B04 D16
INVENTOR(S): BAIRD, E E; DERVAN, P B
PATENT ASSIGNEE(S): (CALY) CALIFORNIA INST OF TECHNOLOGY
COUNTRY COUNT: 82
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 9837087	A1	19980827	(199840)*	EN	74	C07K007-02
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW						
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW						
AU 9861588	A	19980909	(199905)			
EP 973798	A1	20000126	(200010)	EN		
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE						
CN 1260006	A	20000712	(200054)			C12Q001-68
MX 9806945	A1	19990201	(200055)			C07D207-34
JP 2002514205	W	20020514	(200236)		68	C07K007-02
AU 747668	B	20020516	(200244)			C07K007-02

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9837087	A1	WO 1998-US2684	19980213
AU 9861588	A	AU 1998-61588	19980213
EP 973798	A1	EP 1998-906343	19980213
		WO 1998-US2684	19980213
CN 1260006	A	CN 1997-182276	19970721
MX 9806945	A1	MX 1998-6945	19980826

JP 2002514205	W	JP 1998-536723	19980213
		WO 1998-US2684	19980213
AU 747668	B	AU 1998-61588	19980213

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9861588	A	Based on	WO 9837087
EP 973798	A1	Based on	WO 9837087
JP 2002514205	W	Based on	WO 9837087
AU 747668	B	Previous Publ.	AU 9861588
		Based on	WO 9837087

PRIORITY APPLN. INFO: WO 1997-US12722 19970721; WO
1997-US3332 19970220; US
1997-43444P 19970408; US
1997-42022P 19970416; US
1997-837524 19970421; US
1997-853522 19970508; US
1996-607078 19960226

INT. PATENT CLASSIF.:
MAIN: C07D207-34; C07K007-02; C12Q001-68
SECONDARY: A61K031-415; A61K038-00; A61K038-04; A61K041-00; **C07D403-12**; C07H021-02; C07H021-04; C12P019-34; C12Q001-70
ADDITIONAL: C12N015-09

BASIC ABSTRACT:

WO 9837087 A UPAB: 20020711
An improvement in a polyamide which specifically binds to base pairs in the minor groove of a DNA molecule, comprising a positive patch consisting of a rigid group adjacent to a positively charged group such that a positive charge is delivered to the phosphate groove of a DNA molecule, is new.Also claimed are: (1) a tandem linked polyamide having the formula: X1X2X3 gamma (AX6X5X4)LX'6X'5X'4 gamma (X'1X'2X'3)P where gamma is -NH-CH2-CH2CH2-CONH- hairpin linkage derived from gamma -aminobutyric acid or a **chiral** hairpin linkage derived from R-2,4-diaminobutyric acid; X1/X6, X2/X5, X3/X4, X'1/X'6, X'2/X'5, and X'3/X'4 represent carboxyamide binding pairs which bind DNA base pairs and are selected from the group consisting of Hp/Py, Py/Hp, Py/Im, Im/Py, and Py/Py to correspond to the DNA base pair in the minor groove to be bound; L represents an amino acid linking group selected from -alanine and 5-aminovaleric acid (delta); P represents a polyamide selected from X1X2X3 gamma X4X5X6, X1X2X3 gamma X4X5X6X7X8; X1X2X3 gamma X4X5X6X7X8X9X10; and X1X2X3 gamma X4X5X6X7X8X9X10X11X12, where X1-X12 are independently selected from -alanine, pyrrole, hyroxypyrole and imidazole; and A represents a positive patch consisting of a rigid group adjacent to a charged group such that a positive charge is delivered to the phosphate backbone or major groove of a DNA molecule.
USE - The polyamides can be used in a method for inhibiting **gene expression** (claimed).
Dwg.0/18

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B04-C03D; B12-K04A; D05-H18

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YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, TOXCENTER, USPATFULL, WPIX, BIOSIS, CANCERLIT, BIOTECHNO, BIOTECHDS, SCISEARCH' - CONTINUE? (Y)/N:y

YOU HAVE REQUESTED DATA FROM 15 ANSWERS - CONTINUE? Y/(N):y

L89 ANSWER 70 OF 84 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1990:416805 BIOSIS
DOCUMENT NUMBER: PREV199090077606; BA90:77606
TITLE: BIOCHEMICAL CORRELATES OF THE ANTITUMOR AND ANTIMITOCHONDRIAL PROPERTIES OF GOSSYPOL ENANTIOMERS.
AUTHOR(S): BENZ C C [Reprint author]; KENIRY M A; FORD J M; TOWNSEND A J; COX F W; PALAYOOR S; MATLIN S A; HAIT W N; COWAN K H
CORPORATE SOURCE: CANCER RES INST, UNIV CALIF, SAN FRANCISCO, CALIF 94143-0128, USA
SOURCE: Molecular Pharmacology, (1990) Vol. 37, No. 6, pp. 840-847. CODEN: MOPMA3. ISSN: 0026-895X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 17 Sep 1990
Last Updated on STN: 17 Sep 1990

ED Entered STN: 17 Sep 1990
Last Updated on STN: 17 Sep 1990

AB Racemic gossypol has been shown to have antitumor properties that may be due to its ability to uncouple tumor mitochondria or to its inhibitory effects on a variety of nonmitochondrial enzymes. We have studied the antimitochondrial and enzyme-inhibiting properties of gossypol in human carcinoma cell lines of breast (MCF-7, T47-D), ovarian (OVCAR-3) colon (HCT-8), and pancreatic (MiaPaCa) origin by comparing the effects of its purified (+)- and (-)-enantiomers. (-)-Gossypol shows up to 10-fold greater antiproliferative activity than (+)-gossypol in the cancer cell lines and in normal hematopoietic stem cells grown in vitro, with IC50 values ranging from 1.5 to 4.0 μM for the cancer cells and from 10 to 20 μM for the human marrow stem cells. As well, multidrug-resistant MCF/Adr cells appear more resistant to (-)-gossypol than their parental cell line. Electron microscopy indicates that the earliest ultrastructural change in tumor cells exposed to a cytotoxic (10 μM) concentration of (-)-gossypol is the selective destruction of their mitochondria. Consistent with this observation, 31P magnetic resonance spectroscopy detects pronounced changes in tumor cell high energy phosphate metabolism within 24 hr of (-)-gossypol treatment, manifest by 1.6- to >50-fold differential reductions in the intracellular ratios of ATP/Pi, relative to (+)-gossypol-treated cell lines; the magnitude of these antimitochondrial effects correlates with the antiproliferative activity of (-)-gossypol. Northern blot RNA analyses suggest that treatment with a 5-10 μM dose of (-)-gossypol induces a transient increase in the **expression** of heat shock **gene** products, particularly hsp-70 **transcripts.** The mean 5-fold increase in (-)-gossypol-induced hsp-70 mRNA appears coincident with a comparable heat-stimulated increase in transcript levels, as compared with control or (+)-gossypol-treated cells. The enzyme-inhibiting properties of gossypol enantiomers were compared in cell-free assays measuring glutathione-S-transferase-α, -μ, and π activities, calmodulin stimulation of cyclic **nucleotide phosphodiesterase,** and protein kinase C activity. Both enantiomers are near equivalent antagonists of calmodulin stimulation and protein kinase C activity, exceeding the potency of known inhibitors such as phenothiazines by as much as 50-fold. In contrast, (-)-gossypol is a 3-fold more potent inhibitor of glutathione-S-transferase-α and -π isozyme activity, resulting in IC50 values of 1.6 and 7.0 μM, respectively, for these two

isozymes. Because of the enhanced resistance of MCF/Adr cells to (-)-gossypol, which may be related to their increased glutathione-S-transferase and protein kinase C content, (-)-gossypol should be evaluated for its potential to modify the cytotoxic resistance of human carcinoma cells to other chemotherapeutic agents. Furthermore, the above newly described (+)- and (-)-gossypol effects may be useful in directing structure-function studies using **chiral**-specific gossypol derivatives, in order to develop more selective and potent antimitochondrial chemotherapeutic agents.

CC Cytology - Human 02508
Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Enzymes - Chemical and physical 10806
Enzymes - Physiological studies 10808
Pathology - Therapy 12512
Pharmacology - Drug metabolism and metabolic stimulators 22003
Pharmacology - Clinical pharmacology 22005
Neoplasms - Therapeutic agents and therapy 24008

IT Major Concepts
Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Oncology (Human Medicine, Medical Sciences); Pharmacology

IT Miscellaneous Descriptors
HUMAN ANTINEOPLASTIC-DRUG GLUTATHIONE-S-TRANSFERASE PHARMACODYNAMICS

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 303-45-7 (GOSSYPOL)
50812-37-8 (GLUTATHIONE-S-TRANSFERASE)

L89 ANSWER 71 OF 84 CANCERLIT on STN
ACCESSION NUMBER: 95615469 CANCERLIT
DOCUMENT NUMBER: 95615469
TITLE: Antisense research and applications.
AUTHOR: Anonymous
CORPORATE SOURCE: No affiliation given.
SOURCE: Non-serial, (1993) Antisense Research and Applications. Crooke ST, Lebleu B, eds. Boca Raton, FL, CRC Press, 579 p., 1993. .
DOCUMENT TYPE: Book; (MONOGRAPH)
LANGUAGE: English
FILE SEGMENT: Institute for Cell and Developmental Biology
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950608
Last Updated on STN: 19950608

ED Entered STN: 19950608
Last Updated on STN: 19950608

AB It has only recently become accepted that oligonucleotides might have therapeutic utility. Although new to human therapeutics, small, diffusible, untranslated RNA transcripts, termed antisense RNAs, that pair to specific target RNAs at regions of complementarity, occur universally among prokaryotes and eukaryotes, serving to control target RNA function and expression. The antisense oligonucleotides finding therapeutic application are for the most part chemically modified and rendered resistant to nucleases; they also operate by sequence-specific binding to preselected cellular nucleic acids as their target. This book contains chapters by 56 international collaborating authors who survey the whole field of antisense research and its potential applications. The 32

chapters are grouped into nine sections: an introduction to the history and context of antisense drug discovery; a consideration of nucleic acid structure and function in relation to antisense drugs, including discussion of the 5' cap and the use of ribozymes; antisense RNAs occurring naturally; medicinal chemistry of **oligonucleotides**; first generation analogs, including **methylphosphonates**, **phosphorothioates**, alpha-**oligonucleotides**, P-**chiral** analogs, and other reactive derivatives; newer analogs, including those involving heterocyclic base modification, peptide nucleic acids, 2'-O-alkyl derivatives and various designer approaches; mechanisms of action of current synthetic oligonucleotides, which includes a discussion of higher order structures of HIV-1 RNAs as sites of drug action; pharmacokinetics and toxicology, largely of the major first generation drugs; and activities of current antisense drugs, which includes two chapters on antiviral action, one on their application in inflammation research and therapeutics, and one on inhibition of proto-**oncogene expression** in leukemic cells, which appears the CANCERLIT data base with the accession number ICDB/95615470. There is a subject index.

CN 0 (Antineoplastic Agents); 0 (Antiviral Agents); 0 (Oligonucleotides, Antisense)

L89 ANSWER 72 OF 84 CANCERLIT on STN
ACCESSION NUMBER: 90660171 CANCERLIT
DOCUMENT NUMBER: 90660171
TITLE: OLIGODEOXYNUCLEOTIDES AS ANTISENSE INHIBITORS OF **GENE EXPRESSION**: THERAPEUTIC IMPLICATIONS. JUNE 18-21, 1989, ROCKVILLE, MD.
AUTHOR: Anonymous
CORPORATE SOURCE: No affiliation given.
SOURCE: Non-serial, (1989) Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression: Therapeutic Implications. June 18-21, 1989, Rockville, MD, National Cancer Institute, National Institute of Allergy and Infectious Diseases, 1989. .
DOCUMENT TYPE: Book; (MONOGRAPH)
LANGUAGE: English
FILE SEGMENT: Institute for Cell and Developmental Biology
ENTRY MONTH: 199101
ENTRY DATE: Entered STN: 19941107
Last Updated on STN: 19941107

ED Entered STN: 19941107
Last Updated on STN: 19941107

AB A symposium on therapeutic implications of oligodeoxynucleotides as antisense inhibitors of **gene expression**, held June 18-21, 1989, in Rockville, MD, was cosponsored by NCI and the National Institute of Allergy and Infectious Diseases. Speakers' presentations and poster sessions are summarized. Topics include the following: the antisense approach, control of **gene expression** by **oligodeoxynucleotides** covalently linked to intercalating agents, synthesis (DNA-containing **phosphorodithioate internucleotide** linkages, **oligonucleotide** p-**chiral** analogs, covalently linked oligo analogs, **oligoribonucleotides**), oligo analogs as potential therapeutic agents, FDA definitions, progress in pharmacology and toxicology, characterization of oligonucleotide transport into living cells, modification of antisense oligonucleotides to improve cellular uptake, inhibition of expression (translation arrest by oligos, RNase H activity, behavior of alpha and beta oligos, effect of **phosphorothioate** homo-**oligodeoxynucleotides** on herpes simplex virus type

2-induced DNA polymerase), DNA as a site of action (unusual DNA structures in vivo and in vitro, structural basis for specificity in triple helix formation, inhibition of sequence-specific DNA-binding proteins by oligonucleotide-directed triple helix formation, analysis of the sequence selectivity and cellular application of triplex-forming **oligonucleotides** as gene-specific reagents), and applications (**oligonucleoside methylphosphonates**; comparative inhibition by different antisense **oligonucleotide** analogs; inhibition of tick-borne viral encephalitis expression using covalently linked oligonucleotide analogs; optimum targets for antisense inhibition in human c-myc mRNA; inhibition of HIV; inhibition by **phosphorothioate oligodeoxynucleotides** in cell-free, viral, and **oncogene** systems; inhibition of **expression** in trypanosomes).
CN 0 (Oligonucleotides)

L89 ANSWER 73 OF 84 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2001:32416455 BIOTECHNO
TITLE: PNA oligomers as tools for specific modulation of **gene expression**
AUTHOR: Pooga M.; Land T.; Bartfai T.; Langel U.
CORPORATE SOURCE: U. Langel, Dept. Neurochemistry/Toxicology, Arrhenius Laboratory, Stockholm University, S-10691 Stockholm, Sweden.
E-mail: ulangel@scripps.edu
SOURCE: Biomolecular Engineering, (2001), 17/6 (183-192), 67 reference(s)
CODEN: BIENFV ISSN: 1389-0344
PUBLISHER ITEM IDENT.: S1389034401000752
DOCUMENT TYPE: Journal; General Review
COUNTRY: Netherlands
LANGUAGE: English
SUMMARY LANGUAGE: English
ED 20010530
AB Small synthetic molecules that can specifically inhibit translation and/or transcription have shown great promise as potential antisense/antigene drugs. Peptide nucleic acid (PNA), an oligonucleotide mimic, has a non-charged **achiral** polyamide backbone to which the nucleobases are attached. PNA oligomers are extremely stable in biological fluids and they specifically hybridise to DNA or RNA in a complementary manner, forming very strong heteroduplexes. Some of the mRNAs have yet undetermined and possibly long half-lives, successful down regulation of **gene expression** by antisense **oligonucleotides** (ON) requires that the antisense agent is long lived. PNA fulfils this requirement better than **phosphodiester** or phsphorothioate ONs. PNA can inhibit **transcription** and **translation** of respective **genes** by tight binding to DNA or mRNA. First in vitro experiments to specifically down regulate protein expression by PNA have been followed by successful antisense and antigene application of PNA oligomers in vivo. This review discusses the principles of the in vitro and in vivo use of PNA oligonucleotides. Copyright .COPYRGT. 2001 Elsevier Science B.V.

L89 ANSWER 74 OF 84 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2000:30216898 BIOTECHNO
TITLE: Influence of diastereomeric ratios of deoxyribonucleoside phosphoramidites on the synthesis of phosphorothioate oligonucleotides
AUTHOR: Cheruvallath Z.S.; Sasmor H.; Cole D.L.; Ravikumar V.T.

CORPORATE SOURCE: V.T. Ravikumar, Isis Pharmaceuticals, 2292 Faraday Avenue, Carlsbad, CA 92008, United States.
SOURCE: Nucleosides, Nucleotides and Nucleic Acids, (2000), 19/3 (533-543), 36 reference(s)
CODEN: NNNAFY ISSN: 1525-7770
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
ED 20000508
AB Extensive investigations on the influence of diastereomeric ratios of deoxyribonucleoside phosphoramidites on stereo-reproducibility of solid phase synthesis of phosphorothioate oligodeoxyribonucleotides via the phosphoramidite approach indicate that the process is stereoreproducible and under inherent process control.

L89 ANSWER 75 OF 84 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2005-10520 BIOTECHDS
TITLE: New composition comprises an oligomer complementary to and capable of hybridizing to a target nucleic acid and at least one protein, useful for modulating **gene expression** via a RNA interference pathway; using small interfering RNA for **gene expression** inhibition for use in disease **gene** therapy, diagnosis and prevention
AUTHOR: BAKER B F; ELDRUP A B; MANOHARAN M; BHAT B; GRIFFEY R H; SWAYZE E E; CROOKE S T; PRAKASH T P
PATENT ASSIGNEE: BAKER B F; ELDRUP A B; MANOHARAN M; BHAT B; GRIFFEY R H; SWAYZE E E; CROOKE S T; PRAKASH T P
PATENT INFO: US 2005042647 24 Feb 2005
APPLICATION INFO: US 2004-860455 3 Jun 2004
PRIORITY INFO: US 2004-860455 3 Jun 2004; US 1996-659440 6 Jun 1996
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2005-194973 [20]
AB DERWENT ABSTRACT:
NOVELTY - A composition comprises an oligomer complementary to and capable of hybridizing to a selected target nucleic acid and at least one protein comprising at least a portion of a RNA-induced silencing complex (RISC), where the oligomer includes at least one nucleotide having a modification, and the oligomer includes at least one region of **chirally** pure internucleoside linkages or includes at least one region of inverted polarity, is new.

DETAILED DESCRIPTION - A composition comprises an oligomer complementary to and capable of hybridizing to a selected target nucleic acid and at least one protein, the protein comprising at least a portion of a RISC, where the oligomer includes at least one **nucleotide** having a modification comprising a **phosphorothioate**, **phosphorodithioate**, **phosphonate**, **phosphonothioate**, **phosphotriester**, **phosphorothiotriester**, **phosphoramidate**, **phosphorothioamidate**, phosphinate, boronate, alpha-D-arabinofuranosyl, or 2'-5' internucleoside linkage, and the oligomer includes at least one region of **chirally** pure internucleoside linkages or includes at least one region of inverted polarity. INDEPENDENT CLAIMS are also included for the following: (1) an oligomer having at least a first region and a second region where: (a) the first region of the oligomer is complementary to and capable of hybridizing with the second region of the oligomer; (b) at least a portion of the oligomer is complementary to and capable of hybridizing to a selected

target nucleic acid; (c) the oligomer includes at least two **nucleosides** having a modification comprising a **phosphorothioate**, **phosphorodithioate**, **phosphonate**, **phosphonothioate**, **phosphotriester**, **phosphorothiotriester**, **phosphoramidate**, **phosphorothioamidate**, phosphinate, boronate, alpha-D-arabinofuranosyl, or 2'-5' internucleoside linkage; or (d) the oligomer contains at least one region of **chirally** pure internucleoside linkages or includes at least one region of inverted polarity; (2) a pharmaceutical composition comprising the composition and the oligomer above and a pharmaceutical carrier; (3) a method of modulating the expression of a target nucleic acid in a cell; and (4) a method of treating or preventing a disease or disorder associated with a target nucleic acid.

BIOTECHNOLOGY - Preferred Composition: Specifically, the composition comprises a first oligomer and a second oligomer, where: (a) at least a portion of the first oligomer is capable of hybridizing with at least a portion of the second oligomer; (b) at least a portion of the first oligomer is complementary to and capable of hybridizing to a selected target nucleic acid, and (c) at least one of the first or the second oligomers includes at least one **nucleotide** having a modification comprising a **phosphorothioate**, **phosphorodithioate**, **phosphonate**, **phosphonothioate**, **phosphotriester**, **phosphorothiotriester**, **phosphoramidate**, **phosphorothioamidate**, phosphinate, boronate, alpha-D-arabinofuranosyl, or 2'-5' internucleoside linkage; or (d) at least one of the first and the second oligomers contains at least one region of **chirally** pure internucleoside linkages or includes at least one region of inverted polarity. The first and the second oligomers are a complementary pair of siRNA oligomers. They are also an antisense/sense pair of oligomers. The first and second oligomers have 8-80, 10-50, 12-30, 12-24, or 19-23 nucleobases. Preferably, the first oligomer is an antisense oligomer, and the second oligomer is a sense oligomer. The second oligomer hás ribose **nucleotide** units. The first oligomer includes the **nucleotide** having the modification. The **phosphonate** internucleoside linkage is an alkylphosphonate, cyclohexylphosphonate, benzylphosphonate, or phenylphosphonate internucleoside linkage. Preferably, the alkylphosphonate linkage is a methylphosphonate linkage. The phosphotriester internucleoside linkage is a methylphosphotriester, ethylphosphotriester, isopropylphosphotriester, propylphosphotriester, or aminoalkylphosphotriester internucleoside linkage. The phosphotriester internucleoside linkage is an S-alkylphosphorothiotriester, S-arylphosphorothiotriester, O-alkylphosphorothiotriester, or O-arylphosphorothiotriester internucleoside linkage. It is also 3'aminophosphoramidate, aminoalkylphosphoramidate, or aminoalkylphosphorthioamidate internucleoside linkage. The 2'-5' internucleoside linkage is a 2'-5' adenosine linkage, 2'-5' adenosine phosphorothioate linkage, a 2'-5' xyloadenosine linkage, or a linkage of the formula (1) or (2): X = O or S; Y1 = O or S; R = H, OH, OCH3, O-CH2-CH2-NH-C(NH)NH2, or O-CH2-CH2-N(CH3)2; and B1 = adenine, guanine, cytosine, uracil, 5-methyl uracil, or 5-methyl cytosine. The **chirally** pure internucleoside linkage is a **chirally** pure phosphorothioate, alkylphosphonate, phosphotriester, phosphodiesterthioester, or phosphoramidate internucleoside linkage. Preferred Oligomer: Each of the first and the second regions is at least 10 nucleosidic bases. The first region in a 5' to 3' direction is complementary to the second region in a 3' to 5' direction. The oligomer includes a hairpin structure. The first region of the oligomer is spaced from the second region of the oligomer by a third

region, and where the third region comprises at least two nucleosidic bases or a non-nucleosidic base region. Preferred Method: Modulating the expression of a target nucleic acid in a cell comprises contacting the cell with the composition or the oligomer above. Treating or preventing a disease or disorder associated with a target nucleic acid comprises administering to an animal having or predisposed to the disease or disorder an amount of the composition or the oligomer above.

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - The oligomeric composition is useful for modulating **gene expression** via a RNA interference pathway. It can also be used for diagnostics, therapeutics, prophylaxis, as research reagents, and kits. It is also useful for treating or preventing a disease or disorder associated with a target nucleic acid. Tests are described but no results are given.

ADMINISTRATION - Dosage is 0.1 microg - 100 g per kg of body weight. Administration can be through topical (including ophthalmic and to mucous membranes including vaginal and rectal delivery), pulmonary, e.g. by inhalation or insufflation of powders or aerosols, including nebulizer; intratracheal, intranasal, epidermal, transdermal, oral, or parenteral (e.g. intravenous, intraarterial, subcutaneous, intraperitoneal, or intramuscular injection or infusion; intracranial, e.g. intrathecal or intraventricular) routes.

EXAMPLE - No relevant example given. (82 pages)

L89 ANSWER 76 OF 84 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-15322 BIOTECHDS
TITLE: Composition for modulating target **gene expression**, comprising 2 oligomers which comprise modified phosphorous-containing internucleoside linkages, the first oligomer being capable of hybridizing with the second oligomer and to a target;
antisense sequence and RNA interference for use in gene therapy
AUTHOR: BAKER B F; ELDRUP A B; MANOHARAN M; BHAT B; GRIFFEY R; SWAYZE E E; CROOKE S T; PRAKASH T P
PATENT ASSIGNEE: ISIS PHARM INC
PATENT INFO: WO 2004044134 27 May 2004
APPLICATION INFO: WO 2003-US35067 4 Nov 2003
PRIORITY INFO: US 2003-460433 12 Jun 2003; US 2002-423760 5 Nov 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-411707 [38]
AB DERWENT ABSTRACT:

NOVELTY - A composition (C1) comprising 2 oligomers (I) and (II), where a portion of (I) is capable of hybridizing with a portion of (II), a portion of (I) is capable of hybridizing to a selected target nucleic acid, and (I) and (II) include **nucleotides** having modified **phosphorous**-containing internucleoside linkages, or (I) and (II) contains at least 1 region of **chirally** pure internucleoside linkages or includes a region of inverted polarity.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a pharmaceutical composition (III) comprising (I) and a carrier; (2) a pharmaceutical composition comprising C2 and a carrier; (3) an oligomer (IV) having at least a first region and a second region, where the first region is complementary to and capable of hybridizing with the second region of the oligomer, at least a portion of oligomer is complementary to and capable of hybridizing to a selected target nucleic acid, and the oligomer includes at least two **nucleosides** having a modification comprising: a **phosphorothioate**;

phosphorodithioate; phosphonate; phosphonothioate; phosphotriester; phosphorothiotriester; phosphoramidate; phosphorothioamidate; phosphinate; boronate; alpha-D-arabinofuranosyl; or 2'-5' internucleoside linkage; or the oligomer contains at least one region of **chirally** pure internucleoside linkages or includes at least one region of inverted polarity; and (4) a pharmaceutical composition comprising (IV) and a carrier.

BIOTECHNOLOGY - Preferred Composition: The composition comprises a first oligomer (I) and second oligomer (II), where at least a portion of (I) is capable of hybridizing with at least a portion of (II), at least portion of (I) is complementary to and capable of hybridizing to selected target nucleic acid, and at least one of (I) and (II) includes at least one **nucleotide** having a modification comprising: a **phosphorothioate; phosphorodithioate; phosphonate; phosphonothioate; phosphotriester ; phosphorothiotriester; phosphoramidate; phosphorothioamidate;** phosphinate; boronate; alpha-D-arabinofuranosyl; or 2'-5' internucleoside linkage; or at least one of (I) and (II) contains at least one region of **chirally** pure internucleoside linkages or includes at least one region of inverted polarity. A composition (C2) comprising an oligomer complementary to and capable of hybridizing to a selected target nucleic acid and at least one protein, which comprises at least a portion of a RNA-induced silencing complex (RISC), where the oligomer includes at least one **nucleotide** having a modification comprising a **phosphorothioate; phosphorodithioate; phosphonate; phosphonothioate; phosphotriester ; phosphorothiotriester; phosphoramidate; phosphorothioamidate;** phosphinate; boronate; alpha-D-arabinofuranosyl; or 2'-5' internucleoside linkage, or the oligomer includes at least one region of **chirally** pure internucleoside linkages or includes at least one region of inverted polarity. (I) and (II) are a complementary pair of siRNA oligomers or are an antisense/sense pair of oligomers. (I) and (II) has 10-40 nucleotides, preferably 21-24 nucleotides. (I) is an antisense oligomer and (II) is a sense oligomer which has several ribose **nucleotide** units. (I) includes the **nucleotide** having the modification. The **phosphonate** internucleoside linkage is an alkylphosphonate, cyclohexylphosphonate, benzylphosphonate, or phenylphosphonate internucleoside linkage. The alkylphosphonate linkage is a methylphosphonate linkage. The phosphotriester internucleoside linkage is a methylphosphotriester, ethylphosphotriester, isopropylphosphotriester, or propylphosphotriester internucleoside linkage, aminoalkylphosphotriester internucleoside linkage, S-alkylphosphotriester, S-arylphosphotriester, O-alkylphosphotriester, or O-arylphosphotriester internucleotide linkage. The phosphoramidate internucleoside linkage is a 3'aminophosphoramidate, aminoalkylphosphoramidate, or aminoalkylphosphorthioamidate internucleoside linkage. The 2'-5' internucleoside linkage is a 2'-5' adenosine linkage, 2'-5' adenosine phosphorothioate linkage, 2'-5' xyloadenosine linkage, or a linkage of one of the following formulas (F1) or (F2). In formula (F1): X and Y = O or S; R = H, OH, or OCH3; and B = adenine, guanine, cytosine, uracil, 5-methyl uracil, or 5-methyl cytosine. In formula (F2): X, Y, B = as described above; and R = O-CH2-CH2-NH-C(NH)NH2 or O-CH2-CH2-N(CH3)2. The **chirally** pure internucleoside linkage is a **chirally** pure phosphorothioate, alkylphosphonate, phosphotriester, phosphodiesterthioester, or phosphoramidate internucleoside linkage. In (C2), the oligomer is an antisense oligomer and comprises 10-40, preferably 21-24 nucleotides. C2

includes the further oligomer which is complementary to and hybridizable to the oligomer. The further oligomer is a sense oligomer having several ribose nucleotide units. Preferred Oligomer: Each of the first and second regions is at least 10 nucleosidic bases. The first region in a 5'-3' direction is complementary to the second region in a 5'-3' direction. The oligomer includes a hairpin structure. The first region of the oligomer is spaced from the second region of the oligomer by a third region and where the third region comprises at least two nucleosidic bases or non-nucleosidic base region.

ACTIVITY - None given.

MECHANISM OF ACTION - Antisense therapy; Target **gene expression** modulator. Synthetic siRNAs such as ASO: 5'CasteriskTasteriskGasteriskCasteriskTasteriskAGCTTCCGGATasteriskTasteriskTasteriskGasteriskAasterisk3' (116847,PS); Construct A: 5'r(CAAAUCCAGAGGCTAGCAG)dTdT (sense strand,271790,PO) and TdT(GUUUAGGUCUCCGAUCGUC)r5'(antisense Strand,271766,PO); Construct B: 5'd(CasteriskAasteriskAasteriskAasteriskTasteriskCasteriskCasteriskAasteriskGasteriskAasteriskGasteriskGasteriskCasteriskTasteriskAasteriskGasteriskCasteriskAasteriskGasterisk)2'dTdT (sense strand,335389,PO) and dTdT2'(GasteriskTasteriskTasteriskTasteriskAasteriskGasteriskGasteriskTasteriskCasteriskTasteriskCasteriskCasteriskGasteriskAasteriskTasteriskCasteriskGasteriskTasteriskCasterisk)d5' (antisense strand,335390,PO); Construct C: 5'r(CAAAUCCAGAGGCTAGCAG)dTdT (sense strand,271790,PO) and dTdT2'(GasteriskTasteriskTasteriskTasteriskAasteriskGasteriskGasteriskTasteriskCasteriskTasteriskCasteriskCasteriskGasteriskAasteriskTasteriskCasteriskGasteriskTasteriskCasterisk)d5' (antisense strand,335390,PO) were obtained, where Casterisk is 2'-O-methoxyethyl-5-methyl cytosine; Tasterisk is 2'-O-methoxyethyl-5-methyl uracil; Gasterisk is 2'-O-methoxyethyl guanosine; Aasterisk is 2'-O-methoxyethyl adenosine; PO is phosphodiesters; PS is phosphorothioates; asterisk is 2',5'-linked-3'-deoxynucleotides. 1.6 micro-l of 250 micro-M antisense stock solution was combined with 1.6 micro-l of 250 micro-M sense stock solution , 4 micro-l of 5 x universal buffer (500 mM potassium acetate, 150 mM HEPES-KOH, pH 7.4, 10 mM magnesium acetate) and 12.8 micro-l of ultra pure water followed by heating at 90 degreesC for one minute. The reaction was then allowed to cool to ambient temperature for one hour. The final concentration of the duplex was 20 micro-M in 1 x universal buffer (100 mM potassium acetate, 30 mM HEPES-KOH, pH 7.4, 2mM magnesium acetate). T-24 cell line was obtained from American Type Culture Collection was cultured in Dulbecco's modified Eagle's medium (high glucose) (DMEM) supplemented with 10% fetal bovine serum (FBS) and Penicillin-Streptomycin. Twenty-four well dishes were seeded at an initial density of 75000 cells/well on the day prior to transfection and incubated at 37 degreesC, 5% CO2. Synthetic siRNA was delivered to cells (typically at 80-95% confluency) by using a Lipofectin reagent. The siRNA duplexes were incubated with 6 micrograms/ml Lipofectin per 100 nM siRNA in serum free OptiMEM media for 10 minutes and then added to each well. After 4 hours at 37 degreesC, 5% CO2, the media was aspirated from the cells and replaced with DMEM containing 10% FBS and antibiotics and returned to 37degreesC, 5% CO2 until the cells were harvested. Total cellular RNA was harvested at 18-24 hours post-transfection. 150 microl RLT buffer with 1% beta-ME was added to each well of a 24-well plate. The samples were then transferred to a 96-well plate for RNA isolation. Reduction of target (PTEN) mRNA expression was determined by real time RT-PCR. Reverse-transcription was performed, PTEN mRNA expression levels were normalized to c-raf kinase mRNA levels and/or total mRNA levels. The activity of chimeric construct C showed comparable activity to that of the control siRNA construct (siPTEN) whereas chimeric constructs A and B were inactive.

USE - C1 or C2, or (IV) is useful for modulating the expression of a

target nucleic acid in a cell and for treating or preventing a disease or disorder associated with a target nucleic acid (claimed). The oligomeric compounds can be used to elucidate relationships that exist between proteins and a disease state, phenotype or conditions. The methods include detecting or modulating a target peptide comprising contacting a sample, tissue, cell, or organism with the oligomeric compounds and compositions, measuring the nucleic acid or protein level of the target and/or related phenotypic or chemical endpoint at some time after treatment, and optionally comparing the measured value to a non-treated sample or sample treated with a further oligomeric compound. The oligomeric compounds and compositions can additionally be utilized for diagnostics, therapeutics, prophylaxis and as research reagents and kits. The oligomeric compounds and compositions either alone or in combination with other compounds or therapeutics, can be used as tools in differential and/or combinatorial analyses to elucidate expression patterns of a portion or the entire complement of **genes expressed** within cells and tissues. **Expression** patterns within cells or tissues treated with one or more compounds or compositions are compared to control cells or tissues not treated with the compounds or compositions and the patterns produced are analyzed for differential levels of **gene expression** as they pertain, for e.g., to disease association, signaling pathway, cellular localization, expression level, size, structure or function of the genes examined.

ADMINISTRATION - The compositions are administered by topical, oral, parenteral, intrathecal or intraventricular route. Dosages range from 0.01 mg to 100 g/kg body weight.

EXAMPLE - Oligonucleotides were synthesized via solid phase P(III) phosphoramidite chemistry on an automated synthesizer capable of assembling 96 sequences simultaneously in a 96-well format.(105 pages)

L89 ANSWER 77 OF 84 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-15300 BIOTECHDS
TITLE: Oligomer useful for modulating the expression of a target nucleic acid in a cell comprises two regions complementary to each other and a portion that hybridizes the target nucleic acid;
small interfering RNA and antisense oligonucleotide for use in disease prevention and gene therapy
AUTHOR: ALLERSON C; BHAT B; ELDRUP A B; MANOHARAN M; GRIFFEY R; BAKER B F; SWAYZE E E
PATENT ASSIGNEE: ISIS PHARM INC
PATENT INFO: WO 2004041889 21 May 2004
APPLICATION INFO: WO 2003-US35141 4 Nov 2003
PRIORITY INFO: US 2003-489654 25 Jul 2003; US 2002-423760 5 Nov 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-400650 [37]
AB DERWENT ABSTRACT:
NOVELTY - An oligomer (A) comprises at least a first region and a second region. The first region of the oligomer is complementary to and capable of hybridizing with the second region of the oligomer. At least a portion of the oligomer includes at least one polycyclic sugar surrogate complementary to and capable of hybridizing to a selected target nucleic acid.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) a composition (C2) comprising oligomer (a3) complementary to and capable of hybridizing to a selected target nucleic acid and at least one protein, the protein comprises at least a portion of a RNA-induced silencing complex (RISC), the oligomer includes at least one

polycyclic sugar surrogate; and (2) a composition (C1) comprising a first oligomer (a1) and a second oligomer (a2), at least a portion of (a1) is capable of hybridizing with at least a portion of (a2) and is complementary to and capable of hybridizing to a selected target nucleic acid, at least one of (a1) and (a2) includes at least one polycyclic sugar surrogate.

BIOTECHNOLOGY - Preferred Composition: (C1) Further comprises at least one monomer of formula -CH2-CH2-N(-CO-CH2-Bx)-CH(R3)-CO-N(R4)-. (C2) further includes a further oligomer complementary to and hybridizable to the oligomer. Bx = a heterocyclic base moiety; R3 = H or an amino acid side chain; R4 = H or optionally protected hydroxyl or sugar substituent group. Preferred Oligomer: The first and second regions of (A) have at least 10 nucleobases. The first region of (A) in a 5' to 3' direction is complementary to the second region in a 3' to 5' direction is complementary to the second region in 3' to 5' position. The oligomer includes a hairpin structure. The first region of the oligomer is spaced from the second region of the oligomer by third region that optionally comprises at least two nucleosides. Preferred Components: (a1) And (a2) are complementary pair of siRNA oligomers or are antisense/sense pair of oligomers. (a1), (a2) And (a3) has 10-40 (preferably 18-30, especially 21-24) nucleobases. (a1) And the oligomer in (C2), are antisense oligomers. (a2) And the further oligomer, are sense oligomers and has several ribose nucleoside units. (a1) Includes polycyclic sugar surrogate. The polycyclic sugar surrogate is locked nucleic acid (LNA), bicyclic nucleic acid (BNA), tricyclic sugar moiety (TSM) or bicyclic sugar moiety (BSM) (preferably BSM, BNA or tricyclic nucleic acid). The BSM is a compound of formula (I), (II) joined to other nucleoside of formula (ia), (III)-(VIII), or 5'-U-(O-Y-O-V)yO-Y-O-W-3'. The BNA is hexahydro-cyclopenta(b)furan derivative of formula (IX). B = a heterocyclic base moiety; Q1-Q2-Q3- = -CH2-N(R1)-CH2-, -C(=O)-N(R1)-CH2-, -CH2-O-N(R1)- or N(R1)-O-CH2; R1 = 1-12C alkyl or amino protecting group; T3 and T4 = internucleoside linkage attached to G1, H, a hydroxyl protecting group, conjugate group, activated **phosphorus** moiety, covalent attachment to a support medium or internucleoside linkage attached to G1; G1 = a **nucleoside**, nucleotide, nucleoside mimic, oligonucleoside, oligonucleotide or oligonucleotide mimic; R2 = R4; P4 = an internucleoside linkage to an adjacent monomer or optionally protected hydroxyl group; X1 = O, S, NR40, C(R40)2, -NR40-C(R40)2-, -C(R40)-NR40-, -OC(R40)2-, -(CR40)2-O-, -S-C(R40)2, -C(R40)2-S- or -C(R40)2-C(R40)2- (preferably O); Rc - Re = H, optionally protected hydroxy, sugar substituent, an internucleoside linkage to an adjacent monomer or a terminal group; Z4 = O, S or N(Ra); R40 = H, 1-12C alkyl, 2-12C alkenyl, 2-12C alkynyl, hydroxy, 1-12C alkoxy, 2-12C alkenyloxy, carboxy, 1-12C alkoxycarbonyl, 1-12C alkylcarbonyl, formyl, (hetero)aryl, (hetero)aryloxycarbonyl, (hetero)aryloxy, (hetero)arylcarbonyl, amino, mono- and di(1-6C alkyl)amino, carbamoyl, mono- and di(1-6C alkyl)-aminocarbonyl, amino-1-6C alkyl-aminocarbonyl, mono- and di(1-6C alkyl)amino-1-6C alkyl-aminocarbonyl, 1-6C alkyl-carbonylamino, carbamido, 1-6C alkanoyloxy, sulfono, 1-6C alkylsulfonyloxy, nitro, azide, sulfanyl, 1-6C alkylthio or halo (preferably H or 1-6C alkyl); Rb = H, optionally protected hydroxy, sugar substituent, an internucleoside linkage, Rc or R40; Ra = H or R40; CR40R40 = optionally substituted methylene; Rf - Rh = H; X = O, S, NH or N(R1) (preferably O or S); n = 0 or 1; X5 and Y5 = O, S, CH2, C=O, C=S, C=CH2, CHF or CF2; R20 = H, optionally protected OH or sugar substituent; U, V and W = a group of formula (ii) or (iii); y = 0-20; Y = nucleoside bridge; A = -CH2- or -CH2CH2-; R30 and R31 = H, protective group for hydroxyl or internucleoside linkage. Provided that: (1) when one of T3 and T4 is internucleoside linkage attached to G1 then the other is H, hydroxyl protecting group, conjugate group, activated phosphorus moiety, covalent

attachment to a support medium or internucleoside linkage attached to G1; (2) at least one of Rb-Re is an internucleoside linkage; (3) when one of X5 and Y5 is O or S then the other of X5 and Y5 is other than O or S; and (4) when one of X5 and Y5 is C=O or C=S then the other of X5 and Y5 is other than C=O or C=S. One or two pairs of non-geminal substituents selected from Ra-Rh form a second ring system with the atoms to which the substituents are attached and any intervening atoms and the pair of substituents comprise a biradical of 1-8 groups or atoms selected from C(RaRb)-, -C(Ra)=C(Ra)-, -C(Ra)=N-, -O-, -Si(Ra)2-, -S-, -SO2-, -N(Ra)- or -C=Z4. The **nucleoside** is joined by internucleoside linking group selected from **phosphodiester**, **phosphorothioate**, **chiral phosphorothioate**, **phosphorodithioate**, **phosphotriester**, aminoalkylphosphotriester, methyl and other alkyl phosphonate, **chiral** phosphonate, phosphinate, phosphoramidate, thionophosphoramidate, thionoalkylphosphonate, thionoalkylphosphotriester, selenophosphate, boranophosphate or methylene (methylimino) (preferably phosphodiester, phosphorothioate or **chiral** phosphorothioate).

ACTIVITY - None given.

MECHANISM OF ACTION - Target nucleic acid **expression** modulator; **Gene expression** modulator.

USE - For modulating the expression of a target nucleic acid in a cell, and for treating or preventing a diseases or disorder associated with a target nucleic acid (claimed).

ADMINISTRATION - The oligomer is administered at a dosage of 0.01 microg-200 g/kg. Administration is by oral, rectal, topical (including ophthalmic and mucous membranes e.g. vaginal), intratracheal, intranasal, epidermal, transdermal or parenteral (e.g. subcutaneous, intravenous, intraarterial, intraperitoneal, intramuscular, intracranial, intrathecal or intraventricular) routes; or by inhalation, insufflation or infusion.

ADVANTAGE - The oligomer is potent target nucleic acid **expression** modulator and also modulates **gene expression.**

EXAMPLE - No relevant example given. (154 pages)

L89 ANSWER 78 OF 84 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-11554 BIOTECHDS
TITLE: New immunostimulatory nucleic acid molecule having pyrimidine-purine dinucleotide and a chimeric backbone, useful in treating and preventing asthma, allergy, cancer, infectious disease, autoimmune disease or airway remodeling; involving vector-mediated **gene** transfer and **expression** in host cell for use in gene therapy
AUTHOR: KRIEG A M; SAMULOWITZ U; VOLLMER J; UHLMANN E; JURK M; LIPFORD G; RANKIN R
PATENT ASSIGNEE: COLEY PHARM GROUP INC; COLEY PHARM GMBH
PATENT INFO: WO 2004016805 26 Feb 2004
APPLICATION INFO: WO 2003-US25935 19 Aug 2003
PRIORITY INFO: US 2003-447377 14 Feb 2003; US 2002-404479 19 Aug 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-257200 [24]
AB DERWENT ABSTRACT:

NOVELTY - An immunostimulatory nucleic acid molecule comprising an internal pyrimidine-purine (YZ) dinucleotide and chimeric backbone, where one internal YZ dinucleotide has a phosphodiester(-like) internucleotide linkage, where optionally each additional internal YZ dinucleotide has a phosphodiester(-like) or stabilized internucleotide linkage, where other internucleotide linkages are stabilized, is new.

DETAILED DESCRIPTION - An immunostimulatory nucleic acid molecule

comprises at least one internal pyrimidine-purine (YZ) dinucleotide and a chimeric backbone, where at least one internal YZ dinucleotide has a phosphodiester or phosphodiester-like internucleotide linkage, where optionally each additional internal YZ dinucleotide has a phosphodiester, phosphodiester-like or stabilized internucleotide linkage and where all other internucleotide linkages are stabilized. INDEPENDENT CLAIMS are also included for: (1) an oligonucleotide comprising: (a) an immunostimulatory nucleic acid molecule comprising a chimeric backbone and at least one sequence N1YGN2, where independently for each sequence N1YGN2, where YG is an internal pyrimidine-guanosine (YG) dinucleotide and N1 and N2 are each, independent of the other, any nucleotide and where for the at least one sequence N1YGN2 and optionally for each additional sequence N1YGN2, the YG dinucleotide has a phosphodiester or phosphodiester-like internucleotide linkage and N1 and Y and G and N2 are linked by a **phosphodiester** or **phosphodiester**-like internucleotide linkage when N1 and N2 is an internal **nucleotide**, respectively and where all other internucleotide linkages are stabilized; or (b) an octameric sequence comprising at least one YZ dinucleotide having a **phosphodiester** or **phosphodiester**-like internucleotide linkage and at least 4 T **nucleotides**, where Y is a pyrimidine or modified pyrimidine, Z is a guanosine or modified guanosine and where the oligonucleotide includes at least one stabilized internucleotide linkage; (2) modulating an immune response; (3) treating airway remodeling; (4) manufacturing a medicament of an oligonucleotide of (1) for stimulating an immune response; and (5) stimulating an immune response.

BIOTECHNOLOGY - Preferred Nucleic Acid: The immunostimulatory nucleic acid molecule comprises any of the 100 sequences of 14-34 base pairs (bp) (SEQ ID NOS: 1-99 or 241) or any of the 127 sequences of 24 bp (SEQ ID NOS: 105-231). The immunostimulatory nucleic acid molecule is selected from: (a) TasteriskCGasteriskTasteriskCGasteriskTasteriskTasteriskTGasteriskTasteriskCGasteriskTasteriskTasteriskTasteriskGasteriskTasteriskCGasteriskTasteriskT, (b) TasteriskCGasteriskTasteriskCGasteriskTasteriskTasteriskTasteriskTGasteriskTasteriskCGasteriskTasteriskT, (c) TasteriskCGasteriskTasteriskCGasteriskTasteriskTasteriskTasteriskCGasteriskTasteriskCGasteriskTasteriskT, (d) TasteriskGasteriskTasteriskCGasteriskTasteriskTasteriskGasteriskTasteriskCGasteriskTasteriskTGasteriskTasteriskCGasteriskTasteriskTGasteriskTasteriskCGasteriskTasteriskT or (e) TasteriskCGasteriskTasteriskCGasteriskTasteriskTasteriskTasteriskTasteriskCasteriskGasteriskGasteriskCasteriskGasteriskGasteriskCasteriskCasteriskGasteriskCasteriskCasteriskG (SEQ ID NO: 100-104), (f) TasteriskCGTasteriskCGTasteriskTasteriskTasteriskTasteriskGasteriskTasteriskCGTasteriskTasteriskTasteriskTasteriskGasteriskTasteriskCGTasteriskT, (g) TasteriskCGasteriskTCGasteriskTasteriskTasteriskTasteriskTasteriskGasteriskTCGasteriskTasteriskTasteriskTasteriskTasteriskGasteriskTCGasteriskTasteriskT, (h) TasteriskCGTCGTasteriskTasteriskTasteriskTasteriskQasteriskTCGTasteriskTasteriskxasteriskTasteriskGasteriskTCGTasteriskT, (i) TasteriskCasteriskGasteriskTasteriskCasteriskGasteriskTasteriskTasteriskT T GasteriskTasteriskCasteriskGasteriskTasteriskTasteriskT T GasteriskTasteriskCasteriskGasteriskTasteriskT, (j) TasteriskCasteriskGasteriskTasteriskCasteriskGasteriskTasteriskTasteriskTasteriskTGTasteriskCasteriskGasteriskTasteriskTasteriskTasteriskTGTasteriskCasteriskGasteriskTasteriskT, (k) TasteriskCasteriskGasteriskTasteriskCasteriskGasteriskTasteriskTasteriskTT GTasteriskCasteriskGasteriskTasteriskTasteriskTTGTasteriskCasteriskGasteriskTasteriskT, (l) TasteriskCGasteriskTCGasteriskTasteriskTasteriskTTGasteriskTCGasteriskTasteriskTasteriskTTGasteriskTCGasteriskTasteriskT, (m) TasteriskCGTasteriskCGTasteriskTasteriskTasteriskTGTasteriskCGTasteriskTasteriskTasteriskTGTasteriskCGTasteriskT or (n) TasteriskCGTCGTasteriskTasteriskTTGTCGTasteriskTasteriskTTGTCGTasteriskT

(SEQ ID NOS: 232-240). At least one internal YG dinucleotide is CG or TG. The immunostimulatory nucleic acid molecule is a B- or C-Class immunostimulatory nucleic acid molecule. The immunostimulatory nucleic acid molecule is 4-100 nucleotides long. Preferred Oligonucleotide: The oligonucleotide comprises: (a) N1-CG-N2-CG-N3, (b) X1-N1-(GTCGTT)n-N2-X2, (c) 5'TasteriskCasteriskGasteriskTasteriskCGTTTTGAN1CGN2asteriskTasterisk T3' (SEQ ID NO: 296), (d) 5' TasteriskCasteriskGasterisk(Tasterisk/Aaster isk)TN3CGTTTTN4CGN5asteriskTasteriskT 3' (SEQ ID NO: 301), (e) 5'TasteriskCasteriskGasteriskTasteriskCasteriskGNNNCGNCGNNNCasteriskGaste riskNasteriskCasteriskGasteriskTasteriskT3' (SEQ ID NO: 306),(f) 5'TasteriskCGCGN8CGCGCasteriskGN93' (SEQ ID NO: 315), (g) 5TasteriskCG(N6CG N7)2-3TasteriskCGasteriskTasteriskT3' (SEQ ID NOS: 311-312), (h) 5'TasteriskTasteriskGX1X2TGX3X4TasteriskTasteriskTasteriskT asteriskN10TasteriskTasteriskTasteriskTasteriskTasteriskTasteriskT3' (SEQ ID NO: 318), (i) 5' TasteriskCasteriskGasteriskCGasteriskAasteriskCasteri skGasteriskTasteriskTasteriskCGasteriskGasteriskCasteriskGasteriskCJ3aste riskCasteriskGasteriskCasteriskCasteriskG 3' (SEQ ID NO: 321), (j) 5' TCGTCGTTTTGACGTTTTGTCGTT 3' (SEQ ID NO: 368), where N1 to N10 = are each independently a nucleic acid sequence 0-20 nucleotides in length, optionally N6 is one nucleotide, preferably T or A, optionally N7 is five nucleotides, preferably five pyrimidines or TTTTG, N8 to N10 including at least 1-3 CG motif, N8 = PuCGPyPyCG, PuCGPyPyCGCG or ACGTTCG and N9 = CCG; - = an internal phosphodiester or phosphodiester-like internucleotide linkage; asterisk = presence of a stabilized internucleotide linkage; n = 2 or 4-6; and X1 or X2 = are each independently a nucleic acid sequence having **phosphorothioate** internucleotide linkages of 3-10 **nucleotides** or X1 to X4 are independently C or G, where N1(GTCGTT)n-N2 includes at least one phosphodiester internucleotide linkage, where at least one CG dinucleotide has a **phosphodiester** or **phosphodiester** -like internucleotide linkage, where 3' and 5' **nucleotides** of the oligonucleotide do not include a poly-G, poly-A, poly-T or poly-C sequence and where the oligonucleotide is not an antisense oligonucleotide, triple-helix-forming oligonucleotide or ribozyme and the oligonucleotide includes at least 2, 3 or 5 **phosphodiester** internucleotide linkages and optionally the oligonucleotide is 15-40 **nucleotides** in length. The oligonucleotide comprises G-N2-C including 1, 2 or at least 5 stabilized linkages or comprises 5'GNC 3', where N is a nucleic aid sequence of 4-10 nucleotides in length and is at least 50% T and does not include a CG dinucleotide. The nucleic acid has a backbone comprising deoxyribose or ribose. The oligonucleotide further comprises an adjuvant or a cytokine or an antigen. The phosphodiester or phosphodiester-like internucleotide linkage is phosphodiester. The phosphodiester-like linkage is boranophosphonate or diastereomerically pure Rp phosphorothioate. The stabilized internucleotide linkages are selected from phosphorodithioate, methylphosphonate, methylphosphorothioate or a combination, preferably phosphorothioate. The oligonucleotide comprising the sequence in (c) has the one of the following structures: (i) 5'TasteriskCasteriskGasteriskTasteriskCasterisk GasteriskTTTTGAN1CasteriskGasteriskN2asteriskTasteriskT3' (SEQ ID NO: 296), (ii) 5'TasteriskCasteriskGasteriskTasteriskCasteriskGasteriskTaster iskTTTGAN1CasteriskGasteriskN2asteriskTasteriskT3' (SEQ ID NO: 296), (iii) 5'TasteriskCasteriskGasteriskTasteriskCasteriskGasteriskTasteriskTa steriskTasteriskTasteriskGasteriskACCGGTasteriskTasteriskCasteriskGasteri skTasteriskGasteriskTasteriskT3' (SEQ ID NO: 297), (iv) 5'TasteriskCasteriskGasteriskTasteriskCasteriskGasteriskTasteriskTasteris kTasteriskTasteriskGACasteriskGasteriskTasteriskTasteriskTasteriskTasteri skGasteriskTasteriskCasteriskGasteriskTasteriskT3' (SEQ ID NO: 298), (v) 5'TasteriskCasteriskGasteriskTasteriskCasteriskGasteriskTasteriskTTTGaste riskAasteriskCasteriskGasteriskTasteriskTasteriskTasteriskT3' (SEQ ID NO:

299), (vi) 5'TasteriskCasteriskGasteriskTasteriskCasteriskGasteriskTaster
iskTTTGasteriskAasteriskCasteriskGasteriskTasteriskT3' (SEQ ID NO: 300)
or (vii) 5'TasteriskCasteriskGasteriskTasteriskCasteriskGasteriskTasteris
kTasteriskTasteriskTasteriskGAN1CasteriskGasteriskN2asteriskTasteriskT3'
(SEQ ID NO: 296), including at least one CG motif with a phosphodiester
internucleotide linkage. The oligonucleotide comprising the sequence in
(d) has one of the following structures: (i) 5'
TasteriskCasteriskGasterisk(Tasterisk/Aasterisk)TN3CGTTTTN4CasteriskGaste
riskN5asteriskTasteriskT 3', (ii) 5' TasteriskCasteriskGasteriskAasterisk
TasteriskN3CasteriskGasteriskTTTTN4CGasteriskN5asteriskTasteriskT 3',
(iii) 5'TasteriskCasteriskGasteriskTasteriskTasteriskN3CGTTTTN4CGN5asteri
skTasteriskT 3', (iv) 5'TasteriskCasteriskGasteriskAasteriskTasteriskCast
eriskGasteriskTasteriskTasteriskTasteriskTTCGasteriskTasteriskGasteriskCa
steriskGasteriskTasteriskTasteriskTasteriskTasteriskT3' or (v)
5'TasteriskCasteriskGasteriskTasteriskTasteriskTasteriskTasteriskGasteris
kACGTasteriskTasteriskTasteriskTasteriskGasteriskTasteriskCasteriskGaster
iskTasteriskT3' (SEQ ID NOS: 301-305), including at least one CG motif
with a phosphodiester internucleotide linkage. The oligonucleotide
comprising the sequence in (e) has one of the following structure: (i)
5'TasteriskCasteriskGasteriskTasteriskCasteriskGasteriskNasteriskNasteris
kNasteriskCGNCGNasteriskNasteriskNasteriskCasteriskGasteriskNasteriskCast
eriskGasteriskTasteriskT 3', (ii) 5' TasteriskCasteriskGasteriskTasterisk
CasteriskGasteriskTasteriskTasteriskAasteriskCGNCGTasteriskTasteriskAaste
riskCasteriskGasteriskNasteriskCasteriskGasteriskTasteriskT 3', (iii) 5'
TasteriskCasteriskGasteriskTasteriskCasteriskGasteriskNasteriskNasteriskN
asteriskCGTCGNasteriskNasteriskNasteriskCasteriskGasteriskTasteriskCaster
iskGasteriskTasteriskT 3' or (iv) 5'TasteriskCasteriskGasteriskTasteriskC
asteriskGasteriskTasteriskTasteriskAasteriskCGTCGTasteriskTasteriskAaster
iskCasteriskGasteriskTasteriskCasteriskGasteriskTasteriskT 3' (SEQ ID
NOS: 307-310). The oligonucleotide comprising the sequence in (f) has the
following structure: (i) 5'TasteriskCGasteriskCGasteriskAasteriskCGasteri
skTasteriskTasteriskCGasteriskGasteriskCasteriskGasteriskCGasteriskCaster
iskGasteriskCasteriskCasteriskG3' or (ii) 5'TasteriskCasteriskGasteriskCa
steriskGasteriskAasteriskCGasteriskTasteriskTasteriskCasteriskGasteriskCa
steriskGasteriskCGasteriskCasteriskGasteriskCasteriskG3' (SEQ ID NOS: 316
or 317). The oligonucleotide comprising the sequence in (g) has the
following structure: (i) 5'TasteriskCGasteriskTasteriskCGasteriskTasteris
kTasteriskTasteriskTasteriskGasteriskAasteriskCGasteriskTasteriskTasteris
kTasteriskTasteriskGasteriskTasteriskCGasteriskTasteriskT3' or (ii) 5'
TasteriskCGasteriskAasteriskCGasteriskTasteriskTasteriskTasteriskTasteris
kGasteriskTasteriskCGasteriskTasteriskTasteriskTasteriskTasteriskGasteris
kTasteriskCGasteriskTasteriskT 3' (SEQ ID NOS: 313 or 314). The
oligonucleotide comprising the sequence in (h) has the following
structure: (i) 5'TasteriskTasteriskGasteriskCGasteriskTasteriskGasteriskC
GasteriskTasteriskTasteriskTasteriskTasteriskGasteriskAasteriskCGasterisk
TasteriskTasteriskTasteriskTasteriskTasteriskTasteriskT3' or (ii)
5'TasteriskTasteriskGasteriskGCasteriskTasteriskGasteriskGCasteriskTaster
iskTasteriskTasteriskTasteriskGasteriskAasteriskCGasteriskTasteriskTaster
iskTasteriskTasteriskTasteriskTasteriskT3' (SEQ ID NOS: 319 or 320). The
octameric sequence includes a TTTT motif or two YZ dinucleotides, where Y
is an unmethylated C and Z is a guanosine. The octameric sequence is
selected from: (i) TasteriskC-GasteriskTasteriskC-GasteriskTasteriskT,
(ii) C-GasteriskTasteriskC-GasteriskTasteriskTasteriskT, (iii)
GasteriskTasteriskC-GasteriskTasteriskTasteriskTasteriskT, (iv)
TasteriskC-GasteriskTasteriskTasteriskTasteriskTasteriskG, (v)
C-GasteriskTasteriskTasteriskTasteriskTasteriskGasteriskA, (vi)
TasteriskTasteriskTasteriskTasteriskGasteriskAasteriskC-G, (vii)
TasteriskTasteriskTasteriskGasteriskAasteriskC-GasteriskT, (viii)
TasteriskTasteriskGasteriskAasteriskC-GasteriskTasteriskT, (ix)
TasteriskGasteriskAasteriskC-GasteriskTasteriskTasteriskT, (x)

GasteriskAasteriskC-GasteriskTasteriskTasteriskTasteriskT, (xi) AasteriskC-GasteriskTasteriskTasteriskTasteriskTasteriskG, (xii) C-GasteriskTasteriskTasteriskTasteriskTasteriskGasteriskT, (xiii) TasteriskTasteriskTasteriskTasteriskGasteriskTasteriskC-G (xiv) TasteriskTasteriskTasteriskGasteriskTasteriskC-GasteriskT, (xv) GasteriskTasteriskTasteriskTasteriskTasteriskGasteriskTasteriskC or (xvi) TasteriskTasteriskGasteriskTasteriskC-GasteriskTasteriskT. Y is cytosine or a modified cytosine bases, e.g. 5-methyl cytosine, 5-methyl-isocytosine, 5-hydroxy-cytosine, 5-halogeno cytosine, uracil, N4-ethyl-cytosine, 5-fluoro-uracil or hydrogen. Z is guanine or a modified guanine base, e.g. 7-deazaguanine, 7-deaza-7-substituted guanine (such as 7-deaza-7-(C2-C6)alkynylguanine), 7-deaza-8-substituted guanine, hypoxanthine, 2,6-diaminopurine, 2-aminopurme, purine, 8-substituted guanine such as 8-hydroxyguanine, 6-thioguanine, 2-aminopurine or hydrogen. The oligonucleotide has a 3'-3' linkage with one or two accessible 5' ends. The oligonucleotide has two accessible 5' ends, each of which is 5'TCG. The oligonucleotide is a sequence selected from: (i) CGTCGTTTTGACGTTTTGTCGTT, (ii) GTCGTTTTGACGTTTTGTCGTT, (iii) TCGTTTTGACGTTTTGTCGTT, (iv) CGTTTTGACGTTTTGTCGTT, (v) GTTTTGACGTTTTGTCGTT, (vi) TTTTGACGTTTTGTCGTT, (vii) TTTGACGTTTTGTCGTT, (viii) TTGACGTTTTGTCGTT, (ix) TGACGTTTTGTCGTT, (x) GACGTTTTGTCGTT, (xi) ACGTTTTGTCGTT, (xii) GTTTTGTCGTT, (xiii) GTTTTGTCGTT, (xiv) TTTTGTCGTT, (xv) TCGTCGTTTTGACGTTTTGTCGT, (xvi) TCGTCGTTTTGACGTTTTGTCG, (xvii) TCGTCGTTTTGACGTTTTGTC, (xviii) TCGTCGTTTTGACGTTTTGT, (xix) TCGTCGTTTTGACGTTTTG, (xx) TCGTCGTTTTGACGTTTT, (xxi) TCGTCGTTTTGACGTTT, (xxii) TCGTCGTTTTGACGTT, (xxiii) TCGTCGTTTTGACGT, (xxiv) TCGTCGTTTTGACG, (xxv) TCGTCGTTTTGAC, (xxvi) TCGTCGTTTTGA, (xxvii) TCGTCGTTTTG, (xxviii) TCGTCGTTTT, (xxix) CGTCGTTTTGACGTTTTGTCGT, (xxx) GTCGTTTTGACGTTTTGTCG, (xxxi) TCGTTTTGACGTTTTGTC, (xxxii) CGTTTTGACGTTTTGT, (xxxiii) GTTTTGACGTTTTG, (xxxiv) TTTTGACGTTTT or (xxxv) TTTGACGTTT (SEQ ID NOS: 333-367), (xxxvi) TTTGTCGTT, (xxxvii) TTGTCGTT, (xxxviii) TCGTCGTTT, (xxxix) TCGTCGTT or (xl) TTGACGTT. The oligonucleotide is used in the manufacture of a medicament, which includes or does not include an antigen. The oligonucleotide is formulated and is associated with a targeting molecule. Preferred Method: Modulating an immune response comprises administering to a subject an oligonucleotide of (1) in an amount to modulate an immune response. Treating airway remodeling comprises administering to a subject an oligonucleotide comprising a CG dinucleotide, in an amount to treat airway remodeling in the subject. Stimulating an immune response comprises administering to a subject an oligonucleotide of at least 5 nucleotides in length in an amount to stimulate an immune response, where the oligonucleotide includes at least one immunostimulatory dinucleotide motif where the internucleotide linkage between the nucleotides of the dinucleotide has R **chirality** and where at least 70 % of the other internucleotide linkages of the oligonucleotide have S **chirality.**

ACTIVITY - Immunostimulant; Antiasthmatic; Antiallergic; Cytostatic; Immunosuppressive; Respiratory-Gen.; Antimicrobial; Virucide; Antibacterial; Antiparasitic. Three groups of BALB/c mice were injected intraperitoneally with murine renal adenocarcinoma of spontaneous origin (Renca) cells. Each group received either 100 mg semi-soft oligonucleotide SEQ ID NO: 242 or an equivalent volume of phosphate buffer saline (PBS). Mice were followed for survival and tumor size death. Mice which received treatment with PBS had 20 % survival at 50 days and had tumor volumes of 1200 mm3. In contrast, in mice which received semi-soft oligonucleotide treatment had 80 % survival at 50 days and had tumor volumes of 250 mm3.

MECHANISM OF ACTION - Gene Therapy; Vaccine. No biological data given.

USE - The oligonucleotide is useful in stimulating or modulating an

immune response. The medicament shifts the immune response to a Th1 biased response from a Th2 biased response. The oligonucleotide is also useful in the manufacture of a medicament for treating asthma, allergy, cancer, infectious disease, autoimmune disease, airway remodeling or chronic obstructive pulmonary disease or in treating a subject who is a smoker or who is free of symptoms of asthma. The oligonucleotide is useful in inducing cytokine expression, e.g. IL-6 (interleukin-6), TNFalpha (tumor necrosis factor alpha), IFNalpha (interferon-alpha), IFNgamma (interferon-gamma) and IP-10 (Interferon Inducible Protein) (all claimed). The oligonucleotide is also useful in treating and preventing infections caused by viruses, bacteria and parasites.

ADMINISTRATION - Dosage is 0.1 microgram - 10 mg. The medicament is administered with a therapeutic protocol, e.g. surgery, radiation or a medicament and is delivered by oral, nasal, sublingual, intravenous, subcutaneous, mucosal, respiratory, direct injection or dermal routes (claimed).

EXAMPLE - No relevant example given. (276 pages)

L89 ANSWER 79 OF 84 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-22500 BIOTECHDS
TITLE: New composition comprises an oligomer complementary to and capable of hybridizing to target nucleic acid and a protein comprising a portion of a RNA-induced silencing complex, useful for modulating **gene expression** in targeted nucleic acids;
antisense sequence and RNA interference for use in gene therapy
AUTHOR: BAKER B F; ELDRUP A B; MANOHARAN M; BHAT B; GRIFFEY R; SWAYZE E E; CROOKE S T; PRAKASH T P
PATENT ASSIGNEE: BAKER B F; ELDRUP A B; MANOHARAN M; BHAT B; GRIFFEY R; SWAYZE E E; CROOKE S T; PRAKASH T P
PATENT INFO: US 2004171028 2 Sep 2004
APPLICATION INFO: US 2003-700688 4 Nov 2003
PRIORITY INFO: US 2003-700688 4 Nov 2003; US 1996-659440 6 Jun 1996
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-642015 [62]
AB DERWENT ABSTRACT:

NOVELTY - A composition comprises a first oligomer and a second oligomer complementary to and capable of hybridizing to a selected target nucleic acid and at least one protein comprising at least a portion of a RNA-induced silencing complex (RISC), is new.

DETAILED DESCRIPTION - A composition comprises a first oligomer and a second oligomer complementary to and capable of hybridizing to a selected target nucleic acid and at least one protein comprising at least a portion of a RNA-induced silencing complex (RISC), where at least a portion of the first oligomer is capable of hybridizing with at least a portion of the second oligomer; at least a portion of the first oligomer is complementary to and capable of hybridizing to a selected target nucleic acid; at least one of the first or the second oligomers includes at least one **nucleotide** having a modification comprising a **phosphorothioate**, **phosphorodithioate**, **phosphonate**, **phosphonothioate**, **phosphotriester**, **phosphorothiotriester**, **phosphoramidate**, **phosphorothioamidate**, phosphinate, boronate, alpha-D-arabinofuranosyl, or 2'-5' internucleoside linkage; or at least one of the first or the second oligomers contains al least one region of **chirally** pure internucleoside linkages or includes at least one region of inverted polarity. INDEPENDENT CLAIMS are also included for the following: (1) modulating the expression of a target nucleic acid in a

cell; (2) treating or preventing a disease or disorder associated with a target nucleic acid; (3) an oligomer having at least a first region and a second region where the first region of the oligomer is complementary to and capable of hybridizing with the second region of the oligomer; at least a portion of the oligomer is complementary to and capable of hybridizing to a selected target nucleic acid; the oligomer includes at least two **nucleosides** having a modification comprising a **phosphorothioate**, **phosphorodithioate**, **phosphonate**, **phosphonothioate**, **phosphotriester**, **phosphorothiotriester**, **phosphoramidate**, **phosphorothioamidate**, phosphinate, boronate, alpha-D-arabinofuranosyl, or 2'-5' internucleoside linkage; or the oligomer contains at least one region of **chirally** pure internucleoside linkages or includes at least one region of inverted polarity; and (4) a pharmaceutical composition comprising the composition and oligomer above and a pharmaceutical carrier.

BIOTECHNOLOGY - Preferred Composition: The first and the second oligomers are a complementary pair of siRNA oligomers. They are also an antisense/sense pair of oligomers. Each of the first and second oligomers has 10-40 nucleotides, preferably 18-30 or 21-24 nucleotides. The first oligomer is an antisense oligomer and the second oligomer is a sense oligomer. The second oligomer has ribose **nucleotide** units. The first oligomer also includes the **nucleotide** having the modification. The **phosphonate** internucleoside linkage is an alkylphosphonate, cyclohexylphosphonate, benzylphosphonate, or phenylphosphonate internucleoside linkage. The alkylphosphonate linkage is a methylphosphonate linkage. The phosphotriester internucleoside linkage is a methylphosphotriester, ethylphosphotriester, isopropylphosphotriester, or propylphosphotriester internucleoside linkage. The phosphotriester internucleoside linkage is an aminoalkylphosphotriester internucleoside linkage. The phosphotriester internucleoside linkage is an S-alkylphosphorothiotriester, S-arylphosphorothiotriester, O-alkylphosphorothiotriester, or O-arylphosphorothiotriester internucleoside linkage. The phosphoramidate internucleoside linkage is a 3'aminophosphoramidate, aminoalkylphosphoramidate, or aminoalkylphosphorthioamidate internucleoside linkage. The 2'-5' internucleoside linkage is a 2'-5' adenosine linkage, 2'-5' adenosine phosphorothioate linkage, a 2'-5' xyloadenosine linkage, or a linkage of formula (I) or (II). X = O or S; Y = O or S; R = H, OH, or OCH3; and B = adenine, guanine, cytosine, uracil, 5-methyl uracil, or 5-methyl cytosine or X = O or S; Y = O or S; R = O-CH2-CH2-NH-C(NH)NH2, or O-CH2- CH2-N(CH3)2; and B = adenine, guanine, cytosine, uracil, 5-methyl uracil, or 5-methyl cytosine. The **chirally** pure internucleoside linkage is a **chirally** pure phosphorothioate, alkylphosphonate, phosphotriester, phosphodiesterthioester, or phosphorothioamidate internucleoside linkage. Preferred Method: Modulating the expression of a target nucleic acid in a cell comprises contacting the cell with the composition above. Alternatively, modulating the expression of a target nucleic acid in a cell comprises contacting the cell with the oligomer above. Treating or preventing a disease or disorder associated with a target nucleic acid comprises administering to an animal having or predisposed to the disease or disorder an amount of the composition above. Alternatively, treating or preventing a disease or disorder associated with a target nucleic acid comprises administering to an animal having or predisposed to the disease or disorder an amount of the oligomer above. Preferred Oligomer: Each of the first and the second regions is at least 10 nucleosidic bases. The first region in a 5' to 3' direction is complementary to the second region in a 3' to 5' direction. The oligomer includes a hairpin structure. The first region of the oligomer is spaced from the second

region of the oligomer by a third region, where the third region comprises at least two nucleosidic bases. The first region of the oligomer is spaced from the second region of the oligomer by a third region, where the third region comprises a non-nucleosidic base region.

USE - The oligonucleotide compositions are useful for modulating **gene expression** in targeted nucleic acids. They are also useful for diagnostics, therapeutics, prophylaxis, and as research reagents and kits.

ADMINISTRATION - Dosage is 0.01 microg-100 g/kg. Administration can be through topical (including ophthalmic and mucous membranes including vaginal and rectal delivery); pulmonary, e.g. by inhalation or insufflation or powders or aerosols, including by nebulizer; intratracheal; intranasal; epidermal; or transdermal; oral; or parenteral (intravenous, intraarterial, subcutaneous, intraperitoneal, intramuscular, intracranial, or intraventricular) routes.

EXAMPLE - No relevant example given. (63 pages)

L89 ANSWER 80 OF 84 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2002-08325 BIOTECHDS
TITLE: Positively charged oligonucleotides useful for modulating **gene expression**;
triple helix oligonucleotide for gene therapy
AUTHOR: WEEKS D L; DAGLE J
PATENT ASSIGNEE: UNIV IOWA RES FOUND
PATENT INFO: US 6331617 18 Dec 2001
APPLICATION INFO: US 1996-49277 21 Mar 1996
PRIORITY INFO: US 1998-49277 27 Mar 1998
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-096709 [13]
AB DERWENT ABSTRACT:

NOVELTY - Oligonucleotides with cationic phosphoramidate internucleoside or cationic alkylpolyamine internucleoside linkages, and methods of using them to bind nucleic acids to inhibit or alter their expression, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) a triplex-forming oligonucleotide comprising 30% to 100% cationic alkylpolyamine internucleoside linkages; (2) an oligonucleotide (II) comprising at least 30% cationic phosphoramidate internucleoside linkages and at least 4 bases with RNase H sensitive internucleoside linkages positioned between the cationic phosphoramidate internucleoside linkages; (3) a method (III) for cleaving an RNA molecule comprising contacting an RNA molecule in a cell with an oligonucleotide comprising at least 30% cationic phosphoramidate internucleoside linkages and at least 4 bases with RNase H sensitive internucleoside linkages positioned between the cationic phosphoramidate internucleoside linkages (i.e. (II)); (4) a method (IV) for binding an oligonucleotide to a nucleic acid polymer comprising: (a) preparing a triplex-forming oligonucleotide comprising 30% to 100% cationic alkylpolyamine internucleoside linkages (i.e. (I)); and (b) contacting the oligonucleotide with the nucleic acid polymer; (5) a method for limiting **transcription** from a **gene** comprising: (a) preparing a triplex-forming oligonucleotide comprising 30% to 100% cationic alkylpolyamine internucleoside linkages and capable of specifically hybridizing to at least a portion of a gene; and (b) contacting the oligonucleotide with double stranded DNA comprising the gene (the oligonucleotide binds to a portion of the gene to reduce the level of RNA production from the gene); (6) a triplex-forming oligonucleotide (VI) comprising a tag and 30% to 100% cationic alkylpolyamine internucleoside linkages; and (7) a method (VII) for limiting **transcription** from a **gene** comprising: (a) preparing an oligonucleotide comprising at least 1 cationic

alkylpolyamine internucleoside linkage and capable of specifically hybridizing to at least a portion of a gene; and (b) contacting the oligonucleotide with double stranded DNA comprising the gene (the oligonucleotide binds to a portion of the gene to reduce the level of RNA production from the gene).

BIOTECHNOLOGY - Preferred Oligonucleotides: The oligonucleotide (I) comprises: (i) ethylenediamine-class phosphoramidate internucleoside linkages; (ii) dimethylamino propylamine linkages; or (iii) diethylethylenediamine linkages. The triplex forming oligonucleotide (I) may also be a duplex forming oligonucleotide, comprising ethylenediamine-class linkages and mixed **chirality** dimethylamino propylamine linkages and not N,N,N'-trimethylethylenediamine or 4-(2-aminoethyl)morpholine linkages. In particular, it has N-ethylethylenediamine **phosphoramidate** internucleoside linkages or N, N-diethylethylenediamine **phosphoramidate** internucleoside linkages. (I) is at least 12 **nucleotides** in length, and may further comprise at least 1 other modified internucleoside linkage (especially a ethylenediamine phosphoramidate internucleoside linkage or diethylethylenediamine phosphoramidate internucleoside linkage). The oligonucleotide (II) comprises at least 6 bases with RNase H sensitive internucleoside linkages positioned between the cationic phosphoramidate internucleoside linkages. Preferably, there are at least 4 bases with cationic phosphoramidate internucleoside linkages positioned at a 5' end of the oligonucleotide and at least 4 bases with cationic phosphoramidate internucleoside linkages positioned at a 3' end of the oligonucleotide. In (VI) the tag is an enzymatic tag, radiolabeled tag and/or fluorescent tag. Preferred Methods: In (IV) the nucleic acid polymer is RNA or DNA, and may be double stranded or single stranded. (IV) Further comprises denaturing the nucleic acid polymer by exposing the nucleic acid polymer to heat, a denaturing concentration of salt, or a chaotropic agent. In particular: (i) the nucleic acid is DNA and the contacting step forms a triplex; or (ii) the nucleic acid is RNA and the contacting step forms a duplex. (IV) Further comprises introducing the oligonucleotide into a cell. In the method (V) the oligonucleotide binds to a region of the gene (an open reading frame, a promoter or an enhancer). The oligonucleotide used comprises ethylenediamine-class phosphoramidate internucleoside linkages, or dimethylamino propylamine linkages or diethylethylenediamine linkages. The method may further comprise introducing the oligonucleotide into a cell by microinjection and/or lipid-mediated introduction. Preparation: There are a variety of methods known in the art for synthesizing oligonucleotides. Oligonucleotides can be synthesized manually or using automated DNA synthesizers employing H-phosphonate monomers and chemistry. The oligonucleotides disclosed incorporate modified internucleoside linkages. Cationic phosphoramidates are used to replace at least one phosphodiester linkage. Preferably the cationic phosphoramidates are cationic alkyl-polyamine phosphoramidate internucleoside linkages such as ethylenediamine-type internucleoside linkages. In particular, the cationic alkyl-polyamine phosphoramidate internucleoside linkages are N,N-diethyl-ethylenediamine internucleoside linkages, however, other classes of ethylenediamines may also be prepared, including ethylenediamine-type linkages (e.g. diethyl amines such as N-ethyl-ethylenediamine) and diethylethylenediamine linkages. For triplex formation, results have also demonstrated that 3-dimethylamino propylamine linkages can also be used, particularly 3-dimethylamino propylamine linkages with preferably 3 or more consecutive modified linkages. Other cationic phosphoramidates include mixed **chirality** propyl amines such as N, N-diamino propylamine internucleoside linkages. Preferably, the dimethylamino propylamine internucleoside linkages have at least 50% modified internucleoside linkages. Essentially, any compound

that can be added by oxidative amidation to form cationic internucleoside linkages can be tested using the guidelines provided in the specification. Other cationic phosphoramidates suitable as substitutes for phosphodiester internucleoside linkages include diaminobutane and polylysine.

ACTIVITY - None specified.

MECHANISM OF ACTION - Gene therapy; oligonucleotide inhibition; formation of triple and duplex helices. For example, under suitable conditions, an oligonucleotide will bind in the major groove of a DNA duplex. The presence of a third strand may either sterically block transcription, prevent the sequence specific interactions of regulatory proteins with DNA, and/or alter the conformation of the bound duplex. The effect of extensive oligonucleotide modification on triplex formation was examined with oligonucleotides containing 88% modified linkages or 100% cationic phosphoramidate modified linkages (P-3 and P-4, respectively). The ability of oligonucleotides P-3 and P-4 to associate with Duplex I (agttttgtgtccccctctcaggtgtcacag) was compared to that of compounds U-1 and P-2. The assay was performed using 130 mM K+ and 1 mM Mg2+, concentrations that approximated physiologic salt concentrations. The oligonucleotide concentrations used were 20 nM, 200 nM, and 2 .muM. Samples were processed with the various oligonucleotides at the various concentrations and a sample containing no oligonucleotide was used as a background control. Shading in the control lane, located in the region where the triplex band migrated, was subtracted from the triplex bands during data analysis. Triplex formation with U-1 was essentially undetectable under the concentrations tested. Both P-3 and P-4 showed a greater affinity and, therefore, improved stability, for Duplex I than did P-2. The disassociation constants for triplex formation were 8 x 10-7 M for P-2, 1 x 10-7 M for P-4, and 7 x 10-8 M for P-3. The migration of the triplex formed with P-3 was slightly slower than that with P-2, a result of the increased cationic nature of P-3.

USE - The modified oligonucleotides may be used in **gene** therapy protocols to alter **gene expression** by the formation of triple/duplex helical structures. The use of oligonucleotides to form triple helix structures has been previously described (see Moser, et al. (Science, 238:645-650, 1987, and LeDoan, et al., Nucl. Acids Res., 15:7749-7760, 1987).

ADVANTAGE - The oligonucleotides strongly enhance triplex formation even in the presence of K+ ion concentrations exceeding physiologic levels, promote oligonucleotide-mediated duplex formation and can be used for antisense technologies. (1 pages)

L89 ANSWER 81 OF 84 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
ACCESSION NUMBER: 1997-06044 BIOTECHDS
TITLE: Synthesis of chirally pure organophosphorus dinucleotide derivatives;
for oligonucleotide synthesis; use in therapy and as an oligonucleotide DNA probe or RNA probe
AUTHOR: Stec W J; Wozniak L
PATENT ASSIGNEE: Polska-Akademia-Nauk-Centrum-Badan-Molekularnych
LOCATION: Lodz, Poland.
PATENT INFO: WO 9709340 13 Mar 1997
APPLICATION INFO: WO 1996-IB867 29 Aug 1996
PRIORITY INFO: US 1996-653204 24 May 1996; PL 1995-310248 1 Sep 1995
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1997-201912 [18]
AB A method for the synthesis of **chirally** pure nucleoside dimers of chosen sense of P-**chirality** is claimed, which involves: (a) separating a racemic mixture of an amine compound into diastereomers of

chosen and unchosen sense of P-**chirality**; (b) contacting the diastereomers of chosen sense of P-**chirality** with a strong non-**nucleophilic** base and carbon dioxide to give a transient **nucleoside** 3'-O-(Z-substituted)**phosphonoselenoic** or **phosphothioic** acid intermediate; (c) contacting the transient intermediate with an alkylating agent to give a **chirally** pure diastereomer of the chosen sense of P-**chirality**; (d) contacting the resulting diastereomer with a nucleoside under stereospecific coupling conditions to give the **chirally** pure dimer of chosen sense of P-**chirality.** These compounds may be used in the preparation of oligonucleotides, which may be used in diagnostic and therapeutic applications, to: (i) inhibit or alter **expression** of particular **genes** or target sequences in a living cell, allowing selective inactivation, inhibition or alteration of expression; and (ii) to detect the presence of particular nucleic acid target sequences either in vivo or in vitro. (90pp)

L89 ANSWER 82 OF 84 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
ACCESSION NUMBER: 1992-02668 BIOTECHDS
TITLE: Modulation of RNA activity by modifying RNA 5' cap structure; using antisense RNA for regulation of **gene expression**
PATENT ASSIGNEE: Isis-Pharm.
PATENT INFO: WO 9117755 28 Nov 1991
APPLICATION INFO: WO 1991-US3606 22 May 1991
PRIORITY INFO: US 1990-527599 23 May 1990
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1991-368997 [50]
AB A composition for modulating the activity of an RNA comprises: (a) a reactive portion, capable of modifying or removing the 5' cap structure of mRNA; (b) a targeting portion, specifically hybridizable with a preselected nucleotide sequence of the RNA; and (c) a tether for connecting the targeting and reactive portions. The targeting portion is an oligonucleotide (or analog) which specifically hybridizes to the 5' end of the mRNA, or to immature pre-mRNA. The oligonucleotide has 5-50, preferably 15, base units. It also contains either at least one **phosphodiester** bond between **nucleotides** replaced by non-ionic, non-**chiral** linkages, especially a **phosphorothioate** bond. The oligonucleotide is synthetic, and is used as antisense RNA in the **gene expression** field, especially for protein **expression.** The antisense RNA modifies synthesis of undesired proteins which may cause disease or unwanted conditions in animals and humans, by interacting with molecules that direct production of the proteins. The interaction involves inhibition of the maturation, stabilization and/or initiation of translation of a selected mRNA, by modifying the 5' cap structure. (32pp)

L89 ANSWER 83 OF 84 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 96:244406 SCISEARCH
THE GENUINE ARTICLE: UB205
TITLE: NOVEL PHOSPHORAMIDITE MONOMER FOR THE SITE-SELECTIVE INCORPORATION OF A DIASTEREOCHEMICALLY PURE PHOSPHORAMIDATE TO OLIGONUCLEOTIDE
AUTHOR: ENDO M; KOMIYAMA M (Reprint)
CORPORATE SOURCE: UNIV TOKYO, GRAD SCH ENGN, DEPT CHEM & BIOTECHNOL, BUNKYO KU, TOKYO 113, JAPAN (Reprint); UNIV TOKYO, GRAD SCH ENGN, DEPT CHEM & BIOTECHNOL, BUNKYO KU, TOKYO 113, JAPAN
COUNTRY OF AUTHOR: JAPAN

SOURCE: JOURNAL OF ORGANIC CHEMISTRY, (22 MAR 1996) Vol. 61, No. 6, pp. 1994-2000.
ISSN: 0022-3263.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS; LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 29

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Diastereochemically pure dithymidine **phosphoramidates** have been site-selectively incorporated into synthetic **oligonucleotides** by a **phosphoramidite** technique. By using the terminal amino residues bound to the **chiral phosphoramidates**, various functional residues have been attached to the **oligonucleotides** in stereospecific ways. No racemization takes place during these procedures. The dependence of the duplex- and tripler-forming activities of these tethered and functionalized **oligonucleotides** on the diastereochemistry of the **phosphoramidate** is shown.

L89 ANSWER 84 OF 84 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 94:734562 SCISEARCH
THE GENUINE ARTICLE: PR180
TITLE: INTERACTIONS OF OLIGONUCLEOTIDE ANALOGS CONTAINING METHYLPHOSPHONATE INTERNUCLEOTIDE LINKAGES AND 2'-O-METHYLRIBONUCLEOSIDES
AUTHOR: KEAN J M; CUSHMAN C D; KANG H M; LEONARD T E; MILLER P S (Reprint)
CORPORATE SOURCE: JOHNS HOPKINS UNIV, SCH HYG & PUBL HLTH, DEPT BIOCHEM, 615 N WOLFE ST, BALTIMORE, MD, 21205 (Reprint); JOHNS HOPKINS UNIV, SCH HYG & PUBL HLTH, DEPT BIOCHEM, BALTIMORE, MD, 21205
COUNTRY OF AUTHOR: USA
SOURCE: NUCLEIC ACIDS RESEARCH, (25 OCT 1994) Vol. 22, No. 21, pp. 4497-4503.
ISSN: 0305-1048.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 35

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The interactions of **oligonucleotide** analogs, 12-mers, which contain deoxyribo- or 2'-O-methylribose sugars and **methylphosphonate internucleotide** linkages with complementary 12-mer DNA and RNA targets and the effect of **chirality** of the methylphosphonate linkage on oligomer-target interactions was studied. Oligomers containing a single Rp or' Sp methylphosphonate linkage (type 1) or oligomers containing a single phosphodiester linkage at the 5'-end followed by 10 contiguous methylphosphonate linkages of random **chirality** (type 2) were prepared. The deoxyribo- and 2'-O-methylribo- type 1 12-mers formed stable duplexes with both the RNA and DNA as determined by UV melting experiments. The melting temperatures, Tms, of the 2'-O-methylribo-12-mer/RNA duplexes (49 - 53 degrees C) were higher than those of the deoxyribo-12-mer/ RNA duplexes (31 - 36 degrees C). The Tms of the duplexes formed by the Rp isomers of these oligomers were approximately 3 - 5 degrees C higher than those formed by the corresponding Sp isomers. The deoxyribo type 2 12-mer formed a stable duplex, Tm 34 degrees C, with the DNA target and a much less stable duplex with the RNA target, Tm <5 degrees C. In contrast, the 2'-O-methylribo type 2 12-mer formed a stable duplex with the RNA target, Tm 20 degrees C, and a duplex of lower

stability with the DNA target, Tm <5 degrees C. These results show that the previously observed greater stability of oligo-2'-O-methyl **ribonucleotide**/RNA duplexes Versus **oligodeoxyribonucleotide** * /RNA duplexes extends to oligomers containing ***methylphosphonate** linkages and that the configuration of the **methylphosphonate** linkage strongly influences the stability of the duplexes.

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     PASCAL, JICST-EPLUS, CANCERLIT, LIFESCI, DRUGU, EMBASE, SCISEARCH, CABA,
     BIOENG, BIOTECHNO, BIOTECHDS, CONF, CONFSCI' ENTERED AT 13:36:16 ON 19
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L88          14 DUP REM L87 (8 DUPLICATES REMOVED)

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L79             QUE  ABB=ON  PLU=ON  ?POLYETH? OR ?POLYTHIOETH? OR ?PHOSP
                HO? OR (?POLY(1W)(ETH? OR THIO?)) OR ?PHOSPHO?
L86         264 SEA SEGEV, D?/AU
L87          22 SEA L86 AND (?NUCLEO? (15A) (L79 OR PEG))
L88          14 DUP REM L87 (8 DUPLICATES REMOVED)


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L88  ANSWER 1 OF 14  HCAPLUS  COPYRIGHT 2005 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2002:136067  HCAPLUS
DOCUMENT NUMBER:          136:179042
TITLE:                    Poly(ether-thioether)-, poly(ether-sulfoxide)-, and
                          poly(ether-sulfone) nucleic acids, their synthesis and
                          use in medicine and biochemistry
INVENTOR(S):              Segev, David
PATENT ASSIGNEE(S):       Bio-Rad Laboratories, Inc., USA
SOURCE:                   U.S., 46 pp., Cont.-in-part of U.S. Ser. 384,995,
                          abandoned.
                          CODEN: USXXAM
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     US 6348583            B1    20020219    US 1999-411862           19991004
     CA 2382631            AA    20010308    CA 2000-2382631          20000721
     WO 2001016365         A1    20010308    WO 2000-IL432            20000721
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
             YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 1208234            A1    20020529    EP 2000-946256           20000721
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL
     JP 2003508062         T2    20030304    JP 2001-520910           20000721
     AU 769619             B2    20040129    AU 2000-60126            20000721
PRIORITY APPLN. INFO.:                       US 1999-384995      B2   19990830
                                             US 1999-411862      A    19991004
                                             WO 2000-IL432       W    20000721

ED   Entered STN:  21 Feb 2002
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AB A compound comprising a poly(ether-thioether), poly(ether-sulfoxide) or poly(ether-sulfone) backbone bearing a plurality of ligands that are individually bound to chiral carbon atoms located within the backbone, at least one of the ligands including a moiety such as a naturally occurring nucleobase, a nucleobase binding group; a process of synthesizing the compound; monomers to be used in this process and their synthesis; and processes for using the compound in biochem. (e.g., in hybridization) and medicine (e.g., as pharmaceuticals to treat diseases or viral infections) are disclosed.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2001:168182 HCAPLUS
DOCUMENT NUMBER: 134:203476
TITLE: Poly(ether-thioether)-, poly(ether-sulfoxide)-, and poly(ether-sulfone) nucleic acids, their synthesis and use in medicine and biochemistry
INVENTOR(S): **Segev, David**
PATENT ASSIGNEE(S): Bio-Rad Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001016365	A1	20010308	WO 2000-IL432		20000721
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
US 6348583	B1	20020219	US 1999-411862		19991004
CA 2382631	AA	20010308	CA 2000-2382631		20000721
EP 1208234	A1	20020529	EP 2000-946256		20000721
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
JP 2003508062	T2	20030304	JP 2001-520910		20000721
AU 769619	B2	20040129	AU 2000-60126		20000721
PRIORITY APPLN. INFO.:			US 1999-384995	A	19990830
			US 1999-411862	A	19991004
			WO 2000-IL432	W	20000721

OTHER SOURCE(S): MARPAT 134:203476
ED Entered STN: 09 Mar 2001
AB A compound comprising a poly(ether-thioether), poly(ether-sulfoxide) or poly(ether-sulfone) backbone bearing a plurality of ligands that are individually bound to chiral carbon atoms located within the backbone, at least one of the ligands including a moiety such as a naturally occurring nucleobase, a nucleobase binding group; a process of synthesizing the compound; monomers to be used in this process and their synthesis; and processes for using the compound in biochem. (e.g., in hybridization) and medicine (e.g., as pharmaceuticals to treat diseases or viral infections) are disclosed.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 1998:304146 HCAPLUS
DOCUMENT NUMBER: 128:321867
TITLE: Preparation of polyether nucleic acids as gene expression and transcription inhibitors
INVENTOR(S): **Segev, David**
PATENT ASSIGNEE(S): Bio-Rad Laboratories, Inc., USA
SOURCE: Eur. Pat. Appl., 33 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 839830	A1	19980506	EP 1997-308707	19971030
EP 839830	B1	20030122		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 5908845	A	19990601	US 1996-740516	19961030
CA 2217780	AA	19980430	CA 1997-2217780	19971029
JP 10257888	A2	19980929	JP 1997-312866	19971030

PRIORITY APPLN. INFO.: US 1996-740516 A 19961030
OTHER SOURCE(S): MARPAT 128:321867
ED Entered STN: 23 May 1998
AB **Polyether** nucleic acid analogs I [n <1; each B1 = naturally occurring **nucleobase**, **nucleobase** binding group, DNA intercalator; each X1, Y1 = linker group; each C1 = chiral carbon atom; K = first exoconjugate, I = second exoconjugate], compds. comprising a polyether backbone bearing a plurality of ligands that are individually bound to chiral carbon atoms located within said backbone, at least one of said ligands including a moiety selected from the group consisting of a naturally occurring nucleobase, a nucleobase binding group and a DNA intercalator; a process of synthesizing the compound, monomers to be used in this process and their synthesis process and processes for using the compound in biochem. and medicine are described. Thus, protected monomer II was prepared in 6 steps from (S)-(+)-erythrulose hydrate and adenine. Methods for solid-phase synthesis of polyether nucleic acid oligomers are also described.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1994:262372 HCAPLUS
DOCUMENT NUMBER: 120:262372
TITLE: Membrane-linked probes: 5'-(polysulfonylmethyloxyhexaglycol) oligonucleotides
AUTHOR(S): Arad-Yellin, R.; Warshawsky, A.; **Segev, D.**
CORPORATE SOURCE: Dep. Org. Chem., Weizmann Inst. Sci., Rehovot, 76100, Israel
SOURCE: Reactive Polymers (1993), 19(1-2), 67-72
CODEN: REPLEN; ISSN: 0923-1137
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 28 May 1994
AB A novel approach for the synthesis of functional, film-forming polymers

which consists of the assembly of oligonucleotides anchored on a solid support with a soluble polymeric reagent is described. Phosphoramidites of hydroxymethyl-polysulfone and hexaglycoloxymethyl-polysulfone were synthesized and were linked by phosphate ester bonds to fragments of DNA anchored on controlled pore glass supports in the last step of an automatic synthesis of oligonucleotides. Microtiter plates were coated with the oligonucleotide-hexaethyloxymethyl-polysulfone and hybridization with a complementary biotin-labeled DNA probe was applied followed by avidin-peroxidase and detection by the usual procedure. Control expts. using a non-relevant probe for hybridization or using hybridization solns. with no oligonucleotide were also performed.

L88 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 1989:534692 HCAPLUS
DOCUMENT NUMBER: 111:134692
TITLE: Preparation of new nucleotide derivatives as antibacterials and nucleic acid hybridization probes
INVENTOR(S): **Segev, David**
PATENT ASSIGNEE(S): Tamir Biotechnology Ltd., Israel
SOURCE: Eur. Pat. Appl., 57 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 267996	A1	19880525	EP 1986-309090	19861120
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
PRIORITY APPLN. INFO.:			EP 1986-309090	19861120

OTHER SOURCE(S): CASREACT 111:134692
ED Entered STN: 14 Oct 1989
AB The title compds. [I; H, A = NHCO(CH2)xR3; B, B1, B2 = substituted pyrimidine or purine residue, Q; R1 = H, Q1, a labile group removable by acid; R2 = halo, amino, Q2; R3 = NH2, acylamido, biotinamido, dansyl, etc.; R4 = H, alkyl; m, n = 0, integer from 1-1000; q, y = 0, 1; x = 0-21; z = 1-100], useful as antimicrobial agents and nucleic acid hybridization probes, are prepared 2'-Amino-2'-deoxyuridine, prepared from uridine via 2,2'-anhydro-1-(β-D-arabinofuranosyl)uracil and 2'-azido-2'-deoxyuridine, was condensed with biotin to give 2'-biotinamido-2'-deoxyuridine, which was treated with dimethoxytrityl chloride to give 2'-biotinamido-5'-(dimethoxytrityl)-2'-deoxyuridine. This was esterified with MeOPCl2 and the resulting deoxynucleotide derivative was attached through the 3'-OH group to derivatizing, controlled-pore glass, detritylated, and condensed with 5'-(dimethoxytrityl)-2'-**deoxynucleotide**-3'-(Me **phosphorochloridite**). The unreacted, support-bound nucleoside OH groups were then blocked with 1:1 Ac2O/2,6-lutidine and the phosphite was oxidized to the corresponding phosphate. The procedure was repeated as many times as desired to give a deoxyoligonucleotide, from which the terminal DMT groups, the Me group on the phosphate esters, and the protecting groups on the nucleoside base were removed by conventional methods to give modified DNA probes, useful for detecting microorganisms, e.g., avocado sunblotch viroid.

L88 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:595034 HCAPLUS
DOCUMENT NUMBER: 137:151580
TITLE: Oligonucleotide analogs containing linked bases, methods for their synthesis, and their use in

modulating gene expression and treatment of diseases
INVENTOR(S): **Segev, David**
PATENT ASSIGNEE(S): Bio-Rad Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002061110	A2	20020808	WO 2002-IL83	20020129
WO 2002061110	A3	20030206		
WO 2002061110	C1	20031120		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2436665	AA	20020808	CA 2002-2436665	20020129
US 2003191074	A1	20031009	US 2002-57928	20020129
EP 1363640	A2	20031126	EP 2002-711178	20020129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004537503	T2	20041216	JP 2002-561045	20020129
PRIORITY APPLN. INFO.:			US 2001-264308P P	20010129
			WO 2002-IL83 W	20020129

OTHER SOURCE(S): MARPAT 137:151580
ED Entered STN: 09 Aug 2002
AB Nucleic acid and oligonucleotide analogs containing nucleobases attached to chiral carbons in the backbone and containing ≥1 paris of adjacent nucleobases covalently linked together are disclosed. The backbone may be a polyether, e.g., PEG, or polyether derivs. such as poly(ether-thioether), poly(ether-sulfone), and poly(ether-sulfoxide). Linked dimer building blocks and methods for their synthesis as well as methods for solution or solid phase synthesis of the oligo- and polynucleotide analogs are disclosed. The analogs may be used to modulate gene expression and to treat diseases. Thus, the solution phase and solid phase synthesis of PEG-linked oligo-T was demonstrated. The synthesis of a thymidine-linked thymidine dimer with PEG backbone was also shown.

L88 ANSWER 7 OF 14 USPATFULL on STN
ACCESSION NUMBER: 2003:271466 USPATFULL
TITLE: Nucleic acid derivatives
INVENTOR(S): **Segev, David**, Mazkeret Batya, ISRAEL
PATENT ASSIGNEE(S): Bio-Rad Laboratories Inc. (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003191074	A1	20031009	
APPLICATION INFO.:	US 2002-57928	A1	20020129	(10)

	NUMBER	DATE

PRIORITY INFORMATION: US 2001-264308P 20010129 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: G.E. EHRLICH (1995) LTD., c/o ANTHONY CASTORINA, SUITE 207, 2001 JEFFERSON DAVIS HIGHWAY, ARLINGTON, VA, 22202
NUMBER OF CLAIMS: 102
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 33 Drawing Page(s)
LINE COUNT: 2941
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A compound which comprises a backbone having a plurality of chiral carbon atoms, the backbone bearing a plurality of ligands each being individually bound to a chiral carbon atom of the plurality of chiral carbon atoms, the ligands including one or more pair(s) of adjacent ligands each containing a moiety selected from the group consisting of a naturally occurring nucleobase and a nucleobase binding group, wherein moieties of the one or more pair(s) are directly linked to one another via a linker chain; building blocks for synthesizing the compound; and rises of the compound, particularly in antisense therapy.

L88 ANSWER 8 OF 14 USPATFULL on STN
ACCESSION NUMBER: 2002:1319 USPATFULL
TITLE: Structural analogs of amine bases and nucleosides
INVENTOR(S): **Segev, David**, Mazkeret Batya, ISRAEL
PATENT ASSIGNEE(S): Bio-Red Laboratories, Inc., Hercules, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6335432	B1	20020101
APPLICATION INFO.:	US 1998-130373		19980807 (9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Marschel, Ardin H.
NUMBER OF CLAIMS: 40
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 7 Drawing Page(s)
LINE COUNT: 1660
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A compound of a general structure:

D--B--M

wherein:

B is selected from the group consisting of derivatives of naturally occurring nitrogenous bases having a C--H group at positions 5 or 8, and derivatives of nitrogenous base-analogs having a C--H group at positions 5 or 8;

D is at least one derivatizing group, including hydrogen; and

M is a maleimide derivative.

L88 ANSWER 9 OF 14 USPATFULL on STN
ACCESSION NUMBER: 1999:166867 USPATFULL
TITLE: Repair-mediated process for amplifying and detecting nucleic acid sequences
INVENTOR(S): **Segev, David**, Moshav Bne-Rem 40, D. N. Evtah, Israel 79840

PATENT ASSIGNEE(S): Segev, David, United States (U.S. individual)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6004826		19991221
APPLICATION INFO.:	US 1993-155938		19931027 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1992-841649, filed on 20 Feb 1992, now abandoned which is a continuation-in-part of Ser. No. US 1991-784749, filed on 28 Oct 1991, now abandoned which is a continuation of Ser. No. US 1988-221750, filed on 20 Jul 1988, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Arthur, Lisa B.
LEGAL REPRESENTATIVE: Feit, Irving N.Hoffmann & Baron, LLP
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 10 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 2351
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to a process for amplifying and detecting any desired specific nucleic acid sequence that exists in a nucleic acid or mixture thereof. The process comprises treating single strand RNA or separated complementary strands of DNA target with a molar excess of oligonucleotide complement pairs in which these oligonucleotide complement pairs have sequences complementary to the target, under hybridizing conditions. In one embodiment, the oligonucleotide complement pairs may have a gap of one or more bases which may be repaired (filled) by enzymes. The oligonucleotide complement pairs are joined together, forming joined, oligonucleotide product. The target/joined product hybrid nucleic acids are then denatured to single strands again, at which point both the target and the joined products can form hybrids with new oligonucleotide complement pairs. The steps of the reaction may be carried out stepwise or simultaneously and can be repeated as often as desired.

L88 ANSWER 10 OF 14 USPATFULL on STN
ACCESSION NUMBER: 1999:63318 USPATFULL
TITLE: Polyether nucleic acids
INVENTOR(S): **Segev, David**, 10 Hagoren, 76804 Mazkeret Batya, Israel

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5908845		19990601
APPLICATION INFO.:	US 1996-740516		19961030 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Wilson, James O.
LEGAL REPRESENTATIVE: Friedman, Mark M.
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1,14
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 1394
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A compound comprising a polyether backbone bearing a plurality of ligands that are individually bound to chiral carbon atoms located within said backbone, at least one of said ligands including a moiety selected from the group consisting of a naturally occurring nucleobase, a nucleobase binding group and a DNA intercalator; a process of

synthesizing the compound, monomers to be used in this process and their synthesis process and processes for using the compound in biochemistry and medicine.

L88 ANSWER 11 OF 14 USPATFULL on STN
ACCESSION NUMBER: 1998:154027 USPATFULL
TITLE: Chemical process for amplifying and detecting nucleic acid sequences
INVENTOR(S): **Segev, David**, D. N. Evtah, Israel
PATENT ASSIGNEE(S): ImClone Systems Incorporated, New York, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5846709		19981208	
APPLICATION INFO.:	US 1993-77251		19930615	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Martinell, James
LEGAL REPRESENTATIVE: Feit, Irving N., Gallagher, Thomas C., Sheets, Eric J.
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 20 Drawing Figure(s); 20 Drawing Page(s)
LINE COUNT: 1544
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to a method of amplifying and detecting single or double stranded target nucleic acid molecules. Amplification of the target nucleic acid molecule is accomplished by using at least two chemically modified oligonucleotide probes per target nucleic acid molecule to form a joined oligonucleotide product. Each oligonucleotide probe is comprised of a long and short sequence. The long sequence of each probe hybridizes to adjacent regions of the target nucleic acid molecule. The short sequences of each probe hybridize to each other. Chemical functionality groups attached to the short sequences of each oligonucleotide probe covalently combine linking the probes to form a joined oligonucleotide product. The joined oligonucleotide product is formed without the use of enzymes.

The reactivity of the chemical functionality groups on each probe is target dependent. The chemical functionality group on each probe is prevented from reacting with other chemical functionality groups on other probes unless the probes are properly hybridized to the target molecule and to each other, as described above. The chemical functionality groups are covalently attached to the short sequence of each probe in such a way that they are sheltered or protected from the chemical functionality groups of other probes while the probes are in solution. Only when the short sequences of adjacent probes are hybridized to each other are the chemical functionality groups on the probes brought into close enough proximity to form a covalent bond and join the probes to form a joined oligonucleotide product.

L88 ANSWER 12 OF 14 USPATFULL on STN
ACCESSION NUMBER: 1998:150667 USPATFULL
TITLE: Nucleic acid detection and amplification by chemical linkage of oligonucleotides
INVENTOR(S): **Segev, David**, 9A Dov Shamir, 76804 Mazkeret Batya, Israel

	NUMBER	KIND	DATE

PATENT INFORMATION: US 5843650 19981201
APPLICATION INFO.: US 1995-431527 19950501 (8)
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Zitomer, Stephanie W.
ASSISTANT EXAMINER: Fredman, Jeffrey
NUMBER OF CLAIMS: 65
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 30 Drawing Figure(s); 22 Drawing Page(s)
LINE COUNT: 3588
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention and kits are directed to a method of amplifying and detecting single or double-stranded target nucleic acid molecules in a test sample. Amplification is accomplished through the use of a minimum of two oligonucleotide probe complement pairs, wherein members oligonucleotide probes from both pair of oligonucleotide probe complement pairs form a minimum of two oligonucleotide probe pairs, at least one of which is complementary to a given portion of a target nucleic acid sequence which act as template. One of the oligonucleotide probes of each oligonucleotide probe pair have an additional protecting sequence which is not complementary to the target sequence. These additional protecting sequences are preferably complementary to each other. Chemical functionality groups attached to the oligonucleotide probes covalently combine the probes to form a joined oligonucleotide product. The joined oligonucleotide product is formed without the use of enzymes. The reactivity of the chemical functionality groups on each probe is target dependent. The chemical functionality group on each probe is prevented from reacting with other chemical functionality groups on other probes unless the probes are properly hybridized to the target molecule. The chemical functionality groups are covalently attached to the oligonucleotide probes in such a way that they are sheltered or protected from the chemical functionality groups of other probes while the probes are in solution. Only when the oligonucleotide probes of an oligonucleotide probe pair are hybridized to the target sequence are the chemical functionality groups on the probes brought into close enough proximity to form a covalent bond and join the probes to form a joined oligonucleotide product. Once formed, the joined oligonucleotide product is denatured from the target nucleic acid molecule thereby doubling the amount of target sequences originally present in the sample. The process is repeated a desired number of times to produce detectable amounts of joined oligonucleotide products.

L88 ANSWER 13 OF 14 USPATFULL on STN
ACCESSION NUMBER: 95:69205 USPATFULL
TITLE: DNA probe signal amplification
INVENTOR(S): **Segev, David**, 1125 52nd St., Brooklyn, NY, United States 11219
PATENT ASSIGNEE(S): Segev, David, Mazkeret Batya, Israel (non-U.S. individual)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5437977		19950801
APPLICATION INFO.:	US 1992-908584		19920529 (7)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1990-503621, filed on 3 Apr 1990, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Zitomer, Stephanie W.
LEGAL REPRESENTATIVE: Feit, Irving N., Sheets, Eric J.

NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 923
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method for amplifying a signal during the detection of target nucleic acid molecules utilizes a primary oligonucleotide probe that binds to a bridging nucleic acid molecule. The bridging molecule hybridizes to a first developer nucleic acid molecule. Each first developer molecule comprises: (a) a first branch having a sequence of at least two different nucleotides and at least six total nucleotides complementary to a sequence of a first branch of a second developer molecule; (b) a second branch comprising a sequence of at least two different nucleotides and at least six total nucleotides complementary to a sequence of a second branch of the second developer molecule; and (c) a detectable label. In the method, the bridging molecule binds to the primary probe and hybridizes to the first developer molecule; the bound first developer molecule hybridizes to the second developer molecule to form a developer chain; additional first and second developer molecules are added to the chain; and the labeled developer molecules in the developer chain are detected.

L88 ANSWER 14 OF 14 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-224019 [19] WPIX
DOC. NO. CPI: C2000-068275
TITLE: New fluorescent maleimide derivatives of amine bases and nucleosides, useful in the synthesis of fluorescent oligonucleotides.
DERWENT CLASS: B02 B03 D16
INVENTOR(S): **SEGEV, D**
PATENT ASSIGNEE(S): (BIRA) BIO-RAD LAB INC; (BIOR-N) BIO RED LAB INC
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000008041	A1	20000217	(200019)*	EN	78
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: CA JP					
EP 1102782	A1	20010530	(200131)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
US 6335432	B1	20020101	(200207)		
JP 2002522446	W	20020723	(200263)		91

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000008041	A1	WO 1999-US17587	19990804
EP 1102782	A1	EP 1999-940867	19990804
		WO 1999-US17587	19990804
US 6335432	B1	US 1998-130373	19980807
JP 2002522446	W	WO 1999-US17587	19990804
		JP 2000-563674	19990804

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1102782	A1 Based on	WO 2000008041

JP 2002522446 W Based on WO 2000008041

PRIORITY APPLN. INFO: US 1998-130373 19980807
ED 20000419
AB WO 200008041 A UPAB: 20000419
NOVELTY - Fluorescent maleimide derivatives of amine bases and **nucleosides** and their triphosphate and **phosphoramidite** forms, are new.
DETAILED DESCRIPTION - Fluorescent maleimide derivatives of amine bases and nucleosides of formula (I) are new:
X = a group of formula (i)-(v);
R1-R5 = a derivatizing group including H; or
R1 = a group of formula (vi) or (vii);
R6, R7, R8, R12 = a derivatizing group;
TPO = a triphosphate group, and
R13, R14 = H or OH.
USE - (I) are useful in the synthesis of fluorescent oligonucleotides or polynucleotides and as probes in hybridization and sequencing reactions, e.g. in the detection and identification of specific genetic sequences.
ADVANTAGE - Compared with other methods of probe detection, the method provides hybridization sites and fluorescent dye at the same time, and does not use nucleotides which have been coupled via a linker arm to fluorescent dyes.
Dwg.0/3

=> file stnguide
FILE 'STNGUIDE' ENTERED AT 13:59:45 ON 19 MAY 2005
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 13, 2005 (20050513/UP).

=>

```
=> d his ful

     (FILE 'HOME' ENTERED AT 13:26:39 ON 18 MAY 2005)

     FILE 'HCAPLUS' ENTERED AT 13:26:46 ON 18 MAY 2005
L1             1 SEA ABB=ON  PLU=ON  US2002-057928/APPS
                 SAVE TEMP L1 RIL928HCAAPP/A
                 D IALL

     FILE 'STNGUIDE' ENTERED AT 13:27:21 ON 18 MAY 2005

     FILE 'WPIX' ENTERED AT 13:29:18 ON 18 MAY 2005
L2             1 SEA ABB=ON  PLU=ON  US2002-057928/APPS
                 SAVE TEMP L2 RIL928WPIAPP/A
                 D IALL

     FILE 'STNGUIDE' ENTERED AT 13:29:41 ON 18 MAY 2005

     FILE 'REGISTRY' ENTERED AT 13:31:49 ON 18 MAY 2005

     FILE 'HCAPLUS' ENTERED AT 13:31:52 ON 18 MAY 2005
L3               TRA L1 1- RN :       60 TERMS

     FILE 'REGISTRY' ENTERED AT 13:31:55 ON 18 MAY 2005
L4            60 SEA ABB=ON  PLU=ON  L3
                 SAVE TEMP L4 RIL928REGAPP/A
                 D SCAN

     FILE 'STNGUIDE' ENTERED AT 13:32:33 ON 18 MAY 2005
                 D SAVED

     FILE 'LREGISTRY' ENTERED AT 14:54:58 ON 18 MAY 2005
L5               STRUCTURE UPLOADED
L6               STR L5

     FILE 'REGISTRY' ENTERED AT 14:57:06 ON 18 MAY 2005
L7            50 SEA SSS SAM L6

     FILE 'STNGUIDE' ENTERED AT 14:58:29 ON 18 MAY 2005

     FILE 'LREGISTRY' ENTERED AT 14:59:21 ON 18 MAY 2005
L8               STR L6

     FILE 'REGISTRY' ENTERED AT 14:59:50 ON 18 MAY 2005
L9            50 SEA SSS SAM L8

     FILE 'STNGUIDE' ENTERED AT 15:00:26 ON 18 MAY 2005

     FILE 'LREGISTRY' ENTERED AT 15:02:01 ON 18 MAY 2005
L10              STR L8

     FILE 'REGISTRY' ENTERED AT 15:03:31 ON 18 MAY 2005
L11           50 SEA SSS SAM L10

     FILE 'STNGUIDE' ENTERED AT 15:04:27 ON 18 MAY 2005
                 D QUE STAT

     FILE 'LREGISTRY' ENTERED AT 15:04:59 ON 18 MAY 2005
L12              STR L10
```

FILE 'REGISTRY' ENTERED AT 15:05:57 ON 18 MAY 2005
L13 50 SEA SSS SAM L12
D SCAN

FILE 'STNGUIDE' ENTERED AT 15:06:41 ON 18 MAY 2005
D QUE STAT

FILE 'REGISTRY' ENTERED AT 15:09:38 ON 18 MAY 2005
SAVE TEMP L12 RIL928PSK1/Q

FILE 'STNGUIDE' ENTERED AT 15:09:57 ON 18 MAY 2005
D SAVED

FILE 'ZCAPLUS' ENTERED AT 15:41:36 ON 18 MAY 2005
E OLIGONUCLEOTIDES/CT
E POLYNUCLEOTIDES/CT

FILE 'STNGUIDE' ENTERED AT 15:42:13 ON 18 MAY 2005
D SAVED

FILE HOME

FILE HCAPLUS

FILE COVERS 1907 - 18 May 2005 VOL 142 ISS 21
FILE LAST UPDATED: 17 May 2005 (20050517/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE STNGUIDE
FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 13, 2005 (20050513/UP).

FILE WPIX
FILE LAST UPDATED: 17 MAY 2005 <20050517/UP>
MOST RECENT DERWENT UPDATE: 200531 <200531/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE http://thomsonderwent.com/coverage/latestupdates/ <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER

GUIDES, PLEASE VISIT:
http://thomsonderwent.com/support/userguides/ <<<

>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS: http://www.thomsonderwent.com/dwpifv <<<

>>> THE CPI AND EPI MANUAL CODES HAVE BEEN REVISED FROM UPDATE 200501. PLEASE CHECK:
http://thomsonderwent.com/support/dwpiref/reftools/classification/code-rev FOR DETAILS. <<<

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 17 MAY 2005 HIGHEST RN 850605-77-5
DICTIONARY FILE UPDATES: 17 MAY 2005 HIGHEST RN 850605-77-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

FILE LREGISTRY
LREGISTRY IS A STATIC LEARNING FILE

NEW CAS INFORMATION USE POLICIES, ENTER HELP USAGETERMS FOR DETAILS.

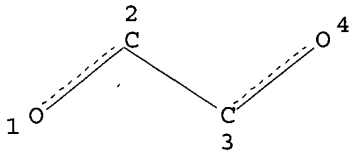
FILE ZCAPLUS

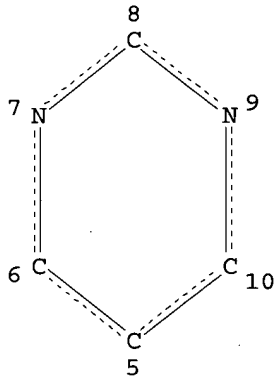
FILE COVERS 1907 - 18 May 2005 VOL 142 ISS 21
FILE LAST UPDATED: 17 May 2005 (20050517/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>
=> d que l5
L5 STR



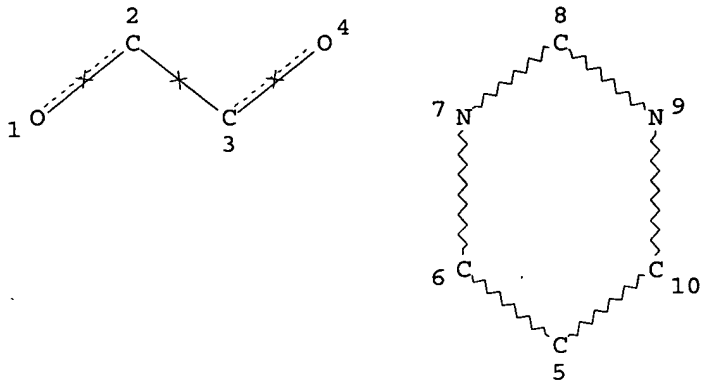


NODE ATTRIBUTES:
NSPEC IS C AT 1
NSPEC IS C AT 2
NSPEC IS C AT 3
NSPEC IS C AT 4
NSPEC IS R AT 5
NSPEC IS R AT 6
NSPEC IS R AT 7
NSPEC IS R AT 8
NSPEC IS R AT 9
NSPEC IS R AT 10
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 1 2 3 4
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

=> d que l6
L6 STR

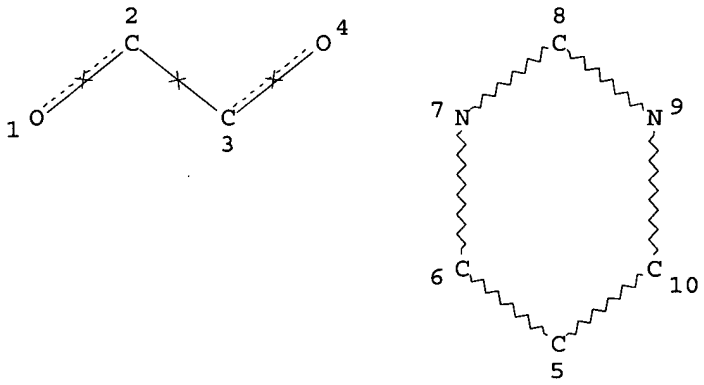


NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 1 2 3 4
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

=> d que l8
L8 STR

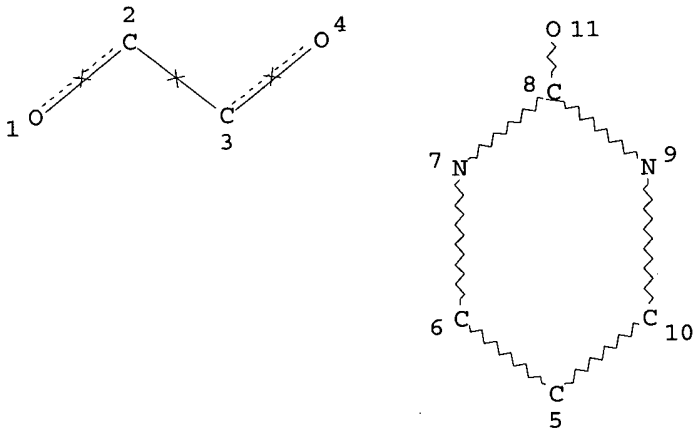


NODE ATTRIBUTES:
CONNECT IS E2 RC AT 1
CONNECT IS E2 RC AT 2
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 1 2 3 4
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

=> d que l10
L10 STR

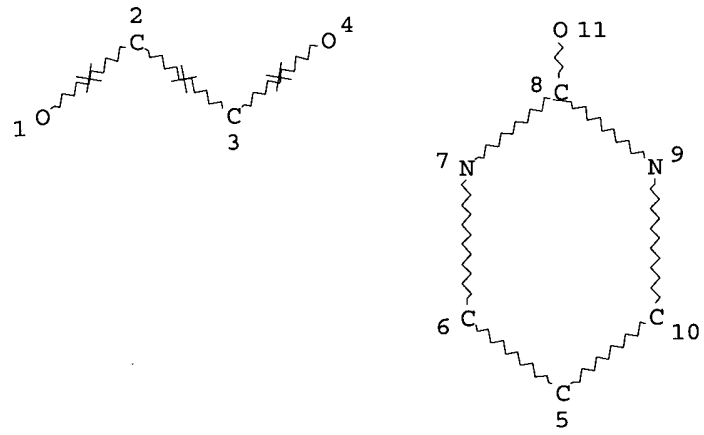


NODE ATTRIBUTES:
CONNECT IS E2 RC AT 1
CONNECT IS E2 RC AT 4
CONNECT IS E1 RC AT 11
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE

=> d que l12
L12 STR



NODE ATTRIBUTES:
NSPEC IS RC AT 1
NSPEC IS RC AT 2
NSPEC IS RC AT 3
NSPEC IS RC AT 4

```
CONNECT IS E2  RC AT   1
CONNECT IS E2  RC AT   4
CONNECT IS E1  RC AT  11
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  11

STEREO ATTRIBUTES: NONE


=> => d his ful

     (FILE 'HOME' ENTERED AT 10:28:59 ON 19 MAY 2005)

     FILE 'HCAPLUS' ENTERED AT 10:29:08 ON 19 MAY 2005
               ACT RIL928HCAAPP/A
               ---------
L1             1 SEA ABB=ON  PLU=ON  US2002-057928/APPS
               ---------

     FILE 'WPIX' ENTERED AT 10:29:23 ON 19 MAY 2005
               ACT RIL928WPIAPP/A
               ---------
L2             1 SEA ABB=ON  PLU=ON  US2002-057928/APPS
               ---------

     FILE 'REGISTRY' ENTERED AT 10:29:39 ON 19 MAY 2005
               ACT RIL928REGAPP/A
               ---------
L3   (         1)SEA ABB=ON  PLU=ON  US2002-057928/APPS
L4               SEL PLU=ON  L3 1- RN :      60 TERMS
L5            60 SEA ABB=ON  PLU=ON  L4
               ---------
               ACT RIL928PSK1/Q
               ---------
L6             STR
               ---------

     FILE 'STNGUIDE' ENTERED AT 10:30:01 ON 19 MAY 2005
               D QUE L6

     FILE 'REGISTRY' ENTERED AT 10:30:53 ON 19 MAY 2005
L7             50 SEA SSS SAM L6
L8         139039 SEA SSS FUL L6
               SAVE TEMP L8 RIL928PSET1/A
L9             25 SEA ABB=ON  PLU=ON  L8 AND L5

     FILE 'STNGUIDE' ENTERED AT 10:33:32 ON 19 MAY 2005
               D SAVED

     FILE 'LREGISTRY' ENTERED AT 10:34:34 ON 19 MAY 2005
L10            STR L6

     FILE 'REGISTRY' ENTERED AT 10:40:14 ON 19 MAY 2005
L11            50 SEA SUB=L8 SSS SAM L10

     FILE 'STNGUIDE' ENTERED AT 10:41:19 ON 19 MAY 2005
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     FILE 'LREGISTRY' ENTERED AT 10:43:50 ON 19 MAY 2005
L12             STR L10

     FILE 'REGISTRY' ENTERED AT 10:45:36 ON 19 MAY 2005
L13           48 SEA SUB=L8 SSS SAM L12
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 10:47:22 ON 19 MAY 2005
                D QUE STAT

     FILE 'REGISTRY' ENTERED AT 10:52:14 ON 19 MAY 2005
L14           962 SEA SUB=L8 SSS FUL L12
                SAVE TEMP L14 RIL928RSET1/A
L15             2 SEA ABB=ON  PLU=ON  L14 AND L5
L16               ANALYZE PLU=ON  L14 1- LC :      16 TERMS
                  D

     FILE 'STNGUIDE' ENTERED AT 10:55:29 ON 19 MAY 2005
                D SAVED

     FILE 'HCAPLUS' ENTERED AT 10:55:52 ON 19 MAY 2005
L17           419 SEA ABB=ON  PLU=ON  L14

     FILE 'ZCAPLUS' ENTERED AT 10:56:49 ON 19 MAY 2005
                E OLIGONUCLEOTIDES/CT
                E POLYNUCLEOTIDES/CT

     FILE 'STNGUIDE' ENTERED AT 10:57:48 ON 19 MAY 2005

     FILE 'HCAPLUS' ENTERED AT 11:08:53 ON 19 MAY 2005
L18             QUE ABB=ON  PLU=ON  ?MODULAT? OR ?MODERAT? OR ?REGULAT? OR
                ?CONTROL?
                SAVE TEMP L18 RIL928MOD/Q
L19             QUE ABB=ON  PLU=ON  ?PROHIB? OR ?INHIB? OR ?REPRESS? OR
                ?SUPPRESS? OR ?DISRUPT? OR ?INTERRUPT? OR BLOCK? OR STOP? OR
                ?RETARD? OR SLOW?
                SAVE TEMP L19 RIL928HIB/Q
L20             QUE ABB=ON  PLU=ON  ?ENCOURAG? OR ?ENHANC? OR ?PROMOT? OR
                ?ACCELERAT? OR ?AMPLIF?
                SAVE TEMP L20 RIL928PRO/Q
L21             QUE ABB=ON  PLU=ON  ?EXPRES? OR ?TRANSCRI? OR ?TRANSLA?
                SAVE TEMP L21 RIL928EXP/Q

     FILE 'STNGUIDE' ENTERED AT 11:11:14 ON 19 MAY 2005
                D SAVED

     FILE 'HCAPLUS' ENTERED AT 11:12:04 ON 19 MAY 2005
L22             2 SEA ABB=ON  PLU=ON  L17 (L) (?GENE? (5A) L21)
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 11:17:04 ON 19 MAY 2005

     FILE 'HCAPLUS' ENTERED AT 11:17:21 ON 19 MAY 2005
                D BIB 1-2

     FILE 'STNGUIDE' ENTERED AT 11:17:21 ON 19 MAY 2005

     FILE 'STNGUIDE' ENTERED AT 11:17:24 ON 19 MAY 2005
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     FILE 'HCAPLUS' ENTERED AT 11:17:59 ON 19 MAY 2005

     FILE 'ZCAPLUS' ENTERED AT 11:18:14 ON 19 MAY 2005
                E POLYNUCLEOTIDES/CT
                E E27+ALL
                E OLIGONUCLEOTIDES/CT
                E E66+ALL
                D COST

     FILE 'HCAPLUS' ENTERED AT 11:19:52 ON 19 MAY 2005
L23         15503 SEA ABB=ON  PLU=ON  POLYNUCLEOTIDES+PFT,NT/CT
L24          4341 SEA ABB=ON  PLU=ON  "NUCLEOTIDES (L) POLY-"+PFT,NT/CT
L25         66771 SEA ABB=ON  PLU=ON  OLIGONUCLEOTIDES+PFT,NT/CT
L26         20253 SEA ABB=ON  PLU=ON  "NUCLEOTIDES (L) OLIGO-"+PFT,NT/CT
L27            49 SEA ABB=ON  PLU=ON  L17 AND (L23 OR L24 OR L25 OR L26)

     FILE 'STNGUIDE' ENTERED AT 11:22:22 ON 19 MAY 2005

     FILE 'HCAPLUS' ENTERED AT 11:25:53 ON 19 MAY 2005
L28        484923 SEA ABB=ON  PLU=ON  ?GENE? (5A) L21
L29             5 SEA ABB=ON  PLU=ON  L28 AND L17
L30          8670 SEA ABB=ON  PLU=ON  L28 AND (L23 OR L24 OR L25 OR L26)
                D SCAN L29

     FILE 'STNGUIDE' ENTERED AT 11:35:47 ON 19 MAY 2005

     FILE 'HCAPLUS' ENTERED AT 11:36:14 ON 19 MAY 2005
L31            29 SEA ABB=ON  PLU=ON  L30 AND ?CHIRAL?
L32           671 SEA ABB=ON  PLU=ON  ?NUCLEOTID? (L) ?CHIRAL?
L33          5852 SEA ABB=ON  PLU=ON  ?NUCLEO? (L) ?CHIRAL?
L34            18 SEA ABB=ON  PLU=ON  L30 AND L33
L35             3 SEA ABB=ON  PLU=ON  L27 AND ?CHIRAL?
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 11:40:18 ON 19 MAY 2005

     FILE 'HCAPLUS' ENTERED AT 11:40:45 ON 19 MAY 2005
L36            24 SEA ABB=ON  PLU=ON  L35 OR L22 OR L29 OR L34
L37            70 SEA ABB=ON  PLU=ON  L36 OR L27
L38            37 SEA ABB=ON  PLU=ON  L27 AND (AY<2002 OR PY<2002 OR PRY<2002)
L39            58 SEA ABB=ON  PLU=ON  L36 OR L38
                D QUE

     FILE 'STNGUIDE' ENTERED AT 11:41:48 ON 19 MAY 2005

     FILE 'HCAPLUS' ENTERED AT 11:42:34 ON 19 MAY 2005
L40            20 SEA ABB=ON  PLU=ON  L36 AND (AY<2002 OR PY<2002 OR PRY<2002)
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 11:43:08 ON 19 MAY 2005

     FILE 'HCAPLUS' ENTERED AT 11:46:01 ON 19 MAY 2005
L41         71237 SEA ABB=ON  PLU=ON  L8
L42          4126 SEA ABB=ON  PLU=ON  L41 AND L28
L43            10 SEA ABB=ON  PLU=ON  L33 AND L42
L44            26 SEA ABB=ON  PLU=ON  L36 OR L43
                SAVE TEMP L44 RIL928HCA1/A

     FILE 'STNGUIDE' ENTERED AT 11:48:35 ON 19 MAY 2005
                D SAVED
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     FILE 'REGISTRY' ENTERED AT 12:45:23 ON 19 MAY 2005
L45           221 SEA ABB=ON  PLU=ON  L14 AND CASREACT/LC
L46           110 SEA ABB=ON  PLU=ON  L14 AND TOXCENTER/LC
L47            45 SEA ABB=ON  PLU=ON  L14 AND USPATFULL/LC

     FILE 'STNGUIDE' ENTERED AT 12:46:30 ON 19 MAY 2005

     FILE 'CASREACT' ENTERED AT 12:47:05 ON 19 MAY 2005
L48            63 SEA ABB=ON  PLU=ON  L45
L49             1 SEA ABB=ON  PLU=ON  L48 AND ?CHIRAL?
                  D SCAN
L50            52 SEA ABB=ON  PLU=ON  L48 AND (AY<2002 OR PY<2002 OR PRY<2002)
L51            63 SEA ABB=ON  PLU=ON  L45/PRO
L52            52 SEA ABB=ON  PLU=ON  L48 AND ?NUCLEO?
L53             1 SEA ABB=ON  PLU=ON  L49 AND ?CHIRAL?/BI,AB
L54             1 SEA ABB=ON  PLU=ON  L48 AND ?CHIRAL?/BI,AB
                  SAVE TEMP L54 RIL928CRX1/A

     FILE 'TOXCENTER' ENTERED AT 12:51:23 ON 19 MAY 2005
L55            54 SEA ABB=ON  PLU=ON  L46
L56             1 SEA ABB=ON  PLU=ON  L55 AND ?CHIRAL?
L57            29 SEA ABB=ON  PLU=ON  L55 AND ?NUCLEO?
L58            29 SEA ABB=ON  PLU=ON  (L56 OR L57)
L59        184644 SEA ABB=ON  PLU=ON  ?GENE? (5A) L21
L60             2 SEA ABB=ON  PLU=ON  L55 AND L59
L61            31 SEA ABB=ON  PLU=ON  L58 OR L60
                  SAVE TEMP L61 RIL928TOX1/A

     FILE 'USPATFULL' ENTERED AT 12:55:02 ON 19 MAY 2005
L62            10 SEA ABB=ON  PLU=ON  L47
                  SAVE TEMP L62 RIL928USP1/A

     FILE 'STNGUIDE' ENTERED AT 12:55:30 ON 19 MAY 2005
                  D SAVED

     FILE 'WPIX' ENTERED AT 12:57:44 ON 19 MAY 2005
L63           365 SEA ABB=ON  PLU=ON  (?NUCLEO? (L) ?CHIRAL?)/BIX
L64         35754 SEA ABB=ON  PLU=ON  ?GENE?/BIX (5A) (?EXPRES?/BIX OR ?TRANSCRI?
                  /BIX OR ?TRANSLA?/BIX)
L65         14875 SEA ABB=ON  PLU=ON  C07D403?/IPC
L66           470 SEA ABB=ON  PLU=ON  C07D498-18/IPC
L67            47 SEA ABB=ON  PLU=ON  L63 AND L64
L68           105 SEA ABB=ON  PLU=ON  L64 AND L65
L69             6 SEA ABB=ON  PLU=ON  L64 AND L66
                  D TRI 1-6
L70           155 SEA ABB=ON  PLU=ON  (L67 OR L68 OR L69)
L71           110 SEA ABB=ON  PLU=ON  L64 AND (L65 OR L66)
L72             2 SEA ABB=ON  PLU=ON  L71 AND L63
                  D TRI 1-2
L73             3 SEA ABB=ON  PLU=ON  L71 AND ?CHIRAL?
L74            73 SEA ABB=ON  PLU=ON  L64 AND ?CHIRAL?
L75         12042 SEA ABB=ON  PLU=ON  (B04-C03C OR C04-C03C)/MC
L76             1 SEA ABB=ON  PLU=ON  L71 AND L75
L77             4 SEA ABB=ON  PLU=ON  L74 AND L75
L78             6 SEA ABB=ON  PLU=ON  L72 OR L73 OR L76 OR L77
                  D TRI 1-6

     FILE 'STNGUIDE' ENTERED AT 13:08:37 ON 19 MAY 2005
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     FILE 'WPIX' ENTERED AT 13:09:42 ON 19 MAY 2005
                SAVE TEMP L78 RIL928WPI1/A

     FILE 'STNGUIDE' ENTERED AT 13:10:05 ON 19 MAY 2005
                D SAVED

     FILE 'HCAPLUS' ENTERED AT 13:13:53 ON 19 MAY 2005
L79             QUE ABB=ON  PLU=ON  ?POLYETH? OR ?POLYTHIOETH? OR ?PHOSPHO? OR
                (?POLY(1W)(ETH? OR THIO?)) OR ?PHOSPHO?

     FILE 'STNGUIDE' ENTERED AT 13:14:19 ON 19 MAY 2005

     FILE 'MEDLINE, BIOSIS, PASCAL, JICST-EPLUS, CANCERLIT, LIFESCI, CABA,
     BIOENG, BIOTECHNO, BIOTECHDS, EMBASE, DRUGU, SCISEARCH' ENTERED AT
     13:18:23 ON 19 MAY 2005
L80        2708486 SEA ABB=ON  PLU=ON  ?GENE? (5A) L21
L81         127825 SEA ABB=ON  PLU=ON  ?NUCLEO? (15A) (L79 OR PEG)
L82            723 SEA ABB=ON  PLU=ON  L81 (L) ?CHIRAL?
L83             31 SEA ABB=ON  PLU=ON  L80 AND L82
L84          12395 SEA ABB=ON  PLU=ON  L80 AND L81
L85             19 DUP REM L83 (12 DUPLICATES REMOVED)
                        ANSWERS '1-2' FROM FILE MEDLINE
                        ANSWER '3' FROM FILE BIOSIS
                        ANSWERS '4-5' FROM FILE CANCERLIT
                        ANSWERS '6-7' FROM FILE BIOTECHNO
                        ANSWERS '8-17' FROM FILE BIOTECHDS
                        ANSWERS '18-19' FROM FILE SCISEARCH
                SAVE TEMP L85 RIL928MUL1/A
                D SAVED

     FILE 'STNGUIDE' ENTERED AT 13:34:51 ON 19 MAY 2005
                D COST

     FILE 'HCAPLUS, CASREACT, TOXCENTER, USPATFULL, WPIX, MEDLINE, BIOSIS,
     PASCAL, JICST-EPLUS, CANCERLIT, LIFESCI, DRUGU, EMBASE, SCISEARCH, CABA,
     BIOENG, BIOTECHNO, BIOTECHDS, CONF, CONFSCI' ENTERED AT 13:36:16 ON 19
     MAY 2005
L86            264 SEA ABB=ON  PLU=ON  SEGEV, D?/AU
L87             22 SEA ABB=ON  PLU=ON  L86 AND (?NUCLEO? (15A) (L79 OR PEG))
L88             14 DUP REM L87 (8 DUPLICATES REMOVED)
                        ANSWERS '1-6' FROM FILE HCAPLUS
                        ANSWERS '7-13' FROM FILE USPATFULL
                        ANSWER '14' FROM FILE WPIX
                SAVE TEMP L88 RIL928MULINV/A
                D SAVED

     FILE 'LREGISTRY' ENTERED AT 13:47:03 ON 19 MAY 2005

     FILE 'REGISTRY' ENTERED AT 13:47:11 ON 19 MAY 2005

     FILE 'ZCAPLUS' ENTERED AT 13:47:15 ON 19 MAY 2005

     FILE 'HCAPLUS' ENTERED AT 13:47:18 ON 19 MAY 2005

     FILE 'CASREACT' ENTERED AT 13:47:21 ON 19 MAY 2005

     FILE 'TOXCENTER' ENTERED AT 13:47:26 ON 19 MAY 2005

     FILE 'USPATFULL' ENTERED AT 13:47:30 ON 19 MAY 2005
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FILE 'WPIX' ENTERED AT 13:47:32 ON 19 MAY 2005

FILE 'MEDLINE' ENTERED AT 13:47:37 ON 19 MAY 2005

FILE 'BIOSIS' ENTERED AT 13:47:42 ON 19 MAY 2005

FILE 'PASCAL' ENTERED AT 13:47:45 ON 19 MAY 2005

FILE 'JICST-EPLUS' ENTERED AT 13:47:49 ON 19 MAY 2005

FILE 'CANCERLIT' ENTERED AT 13:47:54 ON 19 MAY 2005

FILE 'LIFESCI' ENTERED AT 13:47:58 ON 19 MAY 2005

FILE 'DRUGU' ENTERED AT 13:48:04 ON 19 MAY 2005

FILE 'EMBASE' ENTERED AT 13:48:08 ON 19 MAY 2005

FILE 'SCISEARCH' ENTERED AT 13:48:14 ON 19 MAY 2005

FILE 'CONF' ENTERED AT 13:48:17 ON 19 MAY 2005

FILE 'CONFSCI' ENTERED AT 13:48:21 ON 19 MAY 2005

FILE 'CABA' ENTERED AT 13:48:25 ON 19 MAY 2005

FILE 'BIOENG' ENTERED AT 13:48:28 ON 19 MAY 2005

FILE 'BIOTECHNO' ENTERED AT 13:48:35 ON 19 MAY 2005

FILE 'BIOTECHDS' ENTERED AT 13:48:41 ON 19 MAY 2005

FILE 'STNGUIDE' ENTERED AT 13:48:45 ON 19 MAY 2005
           D QUE L44
           D QUE NOS L54
           D QUE NOS L61
           D QUE NOS L62
           D QUE L78
           D QUE L85

FILE 'HCAPLUS, CASREACT, TOXCENTER, USPATFULL, WPIX, MEDLINE, BIOSIS,
CANCERLIT, BIOTECHNO, BIOTECHDS, SCISEARCH' ENTERED AT 13:50:18 ON 19 MAY
2005
L89         84 DUP REM L44 L54 L61 L62 L78 L85 (9 DUPLICATES REMOVED)
                ANSWERS '1-26' FROM FILE HCAPLUS
                ANSWERS '27-54' FROM FILE TOXCENTER
                ANSWERS '55-64' FROM FILE USPATFULL
                ANSWERS '65-69' FROM FILE WPIX
                ANSWER '70' FROM FILE BIOSIS
                ANSWERS '71-72' FROM FILE CANCERLIT
                ANSWERS '73-74' FROM FILE BIOTECHNO
                ANSWERS '75-82' FROM FILE BIOTECHDS
                ANSWERS '83-84' FROM FILE SCISEARCH
           D IBIB ED AB HITIND HITSTR

FILE 'STNGUIDE' ENTERED AT 13:51:28 ON 19 MAY 2005

FILE 'HCAPLUS, TOXCENTER, USPATFULL, WPIX, BIOSIS, CANCERLIT, BIOTECHNO,
BIOTECHDS, SCISEARCH' ENTERED AT 13:52:05 ON 19 MAY 2005
           D IBIB ED AB HITIND HITSTR 2-26
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FILE 'STNGUIDE' ENTERED AT 13:52:33 ON 19 MAY 2005

FILE 'HCAPLUS, TOXCENTER, USPATFULL, WPIX, BIOSIS, CANCERLIT, BIOTECHNO, BIOTECHDS, SCISEARCH' ENTERED AT 13:53:37 ON 19 MAY 2005
D IBIB ED AB HITSTR HITIND 27

FILE 'STNGUIDE' ENTERED AT 13:53:46 ON 19 MAY 2005

FILE 'HCAPLUS, TOXCENTER, USPATFULL, WPIX, BIOSIS, CANCERLIT, BIOTECHNO, BIOTECHDS, SCISEARCH' ENTERED AT 13:54:21 ON 19 MAY 2005
D IBIB ED AB HITIND 28-54

FILE 'STNGUIDE' ENTERED AT 13:54:23 ON 19 MAY 2005

FILE 'HCAPLUS, TOXCENTER, USPATFULL, WPIX, BIOSIS, CANCERLIT, BIOTECHNO, BIOTECHDS, SCISEARCH' ENTERED AT 13:55:51 ON 19 MAY 2005
D IBIB ED AB HITSTR 55-64

FILE 'STNGUIDE' ENTERED AT 13:56:04 ON 19 MAY 2005

FILE 'HCAPLUS, TOXCENTER, USPATFULL, WPIX, BIOSIS, CANCERLIT, BIOTECHNO, BIOTECHDS, SCISEARCH' ENTERED AT 13:56:30 ON 19 MAY 2005

FILE 'STNGUIDE' ENTERED AT 13:56:43 ON 19 MAY 2005

FILE 'HCAPLUS, TOXCENTER, USPATFULL, WPIX, BIOSIS, CANCERLIT, BIOTECHNO, BIOTECHDS, SCISEARCH' ENTERED AT 13:56:53 ON 19 MAY 2005
D IALL ABEQ TECH ABEX 65-69

FILE 'STNGUIDE' ENTERED AT 13:56:59 ON 19 MAY 2005

FILE 'HCAPLUS, TOXCENTER, USPATFULL, WPIX, BIOSIS, CANCERLIT, BIOTECHNO, BIOTECHDS, SCISEARCH' ENTERED AT 13:58:11 ON 19 MAY 2005
D IBIB ED AB HITIND 70-

FILE 'STNGUIDE' ENTERED AT 13:58:20 ON 19 MAY 2005

FILE 'STNGUIDE' ENTERED AT 13:59:09 ON 19 MAY 2005
D QUE L88

FILE 'HCAPLUS, USPATFULL, WPIX' ENTERED AT 13:59:28 ON 19 MAY 2005
D IBIB ED AB L88 1-14

FILE 'STNGUIDE' ENTERED AT 13:59:32 ON 19 MAY 2005

FILE 'STNGUIDE' ENTERED AT 13:59:45 ON 19 MAY 2005

FILE HOME

FILE HCAPLUS

of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 19 May 2005 VOL 142 ISS 21
FILE LAST UPDATED: 18 May 2005 (20050518/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE WPIX
FILE LAST UPDATED: 17 MAY 2005 <20050517/UP>
MOST RECENT DERWENT UPDATE: 200531 <200531/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE http://thomsonderwent.com/coverage/latestupdates/ <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER GUIDES, PLEASE VISIT:
http://thomsonderwent.com/support/userguides/ <<<

>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS: http://www.thomsonderwent.com/dwpifv <<<

>>> THE CPI AND EPI MANUAL CODES HAVE BEEN REVISED FROM UPDATE 200501. PLEASE CHECK:
http://thomsonderwent.com/support/dwpiref/reftools/classification/code-rev FOR DETAILS. <<<

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 18 MAY 2005 HIGHEST RN 850688-83-4
DICTIONARY FILE UPDATES: 18 MAY 2005 HIGHEST RN 850688-83-4

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*
****

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

FILE STNGUIDE
FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 13, 2005 (20050513/UP).

FILE LREGISTRY
LREGISTRY IS A STATIC LEARNING FILE

NEW CAS INFORMATION USE POLICIES, ENTER HELP USAGETERMS FOR DETAILS.

FILE ZCAPLUS

FILE COVERS 1907 - 19 May 2005 VOL 142 ISS 21
FILE LAST UPDATED: 18 May 2005 (20050518/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE CASREACT

FILE CONTENT:1840 - 15 May 2005 VOL 142 ISS 20

New CAS Information Use Policies, enter HELP USAGETERMS for details.

```
**********************************************************
*                                                        *
*     CASREACT now has more than 9.2 million reactions   *
*                                                        *
**********************************************************
```

Some CASREACT records are derived from the ZIC/VINITI database (1974-1991) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE TOXCENTER

FILE COVERS 1907 TO 17 May 2005 (20050517/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TOXCENTER has been enhanced with new files segments and search fields. See HELP CONTENT for more information.

TOXCENTER thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary. See http://www.nlm.nih.gov/mesh/ and http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html for a description of changes.

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 17 May 2005 (20050517/PD)
FILE LAST UPDATED: 17 May 2005 (20050517/ED)
HIGHEST GRANTED PATENT NUMBER: US6895596
HIGHEST APPLICATION PUBLICATION NUMBER: US2005102725
CA INDEXING IS CURRENT THROUGH 17 May 2005 (20050517/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 17 May 2005 (20050517/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2005

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE MEDLINE
FILE LAST UPDATED: 18 MAY 2005 (20050518/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 18 May 2005 (20050518/ED)

FILE RELOADED: 19 October 2003.

FILE PASCAL
FILE LAST UPDATED: 17 MAY 2005 <20050517/UP>
FILE COVERS 1977 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE
IN THE BASIC INDEX (/BI) FIELD <<<

FILE JICST-EPLUS
FILE COVERS 1985 TO 16 MAY 2005 (20050516/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE CANCERLIT
FILE COVERS 1963 TO 15 Nov 2002 (20021115/ED)

On July 28, 2002, CANCERLIT was reloaded. See HELP RLOAD for details.

CANCERLIT thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2002 vocabulary. Enter HELP THESAURUS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE LIFESCI
FILE COVERS 1978 TO 16 May 2005 (20050516/ED)

FILE CABA
FILE COVERS 1973 TO 6 May 2005 (20050506/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

The CABA file was reloaded 7 December 2003. Enter HELP RLOAD for details.

FILE BIOENG
FILE LAST UPDATED: 18 MAY 2005 <20050518/UP>
FILE COVERS 1960 TO DATE

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN
THE BASIC INDEX <<<

FILE BIOTECHNO

FILE LAST UPDATED: 7 JAN 2004 <20040107/UP>
FILE COVERS 1980 TO 2003.

>>> BIOTECHNO IS NO LONGER BEING UPDATED AS OF 2004 <<<

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN /CT AND BASIC INDEX <<<

FILE BIOTECHDS
FILE LAST UPDATED: 13 MAY 2005 <20050513/UP>

>>> USE OF THIS FILE IS LIMITED TO BIOTECH SUBSCRIBERS <<<

>>> NEW CLASSIFICATION SYSTEM FROM 2002 ONWARDS - SEE HELP CLA <<<

>>> NEW DISPLAY FIELDS LS AND LS2 (LEGAL STATUS DATA FROM THE INPADOC DATABASE) AVAILABLE - SEE NEWS <<<

FILE EMBASE
FILE COVERS 1974 TO 12 May 2005 (20050512/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE DRUGU
FILE LAST UPDATED: 16 MAY 2005 <20050516/UP>
>>> DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<
>>> THESAURUS AVAILABLE IN /CT <<<

FILE SCISEARCH
FILE COVERS 1974 TO 12 May 2005 (20050512/ED)

FILE CONF
FILE LAST UPDATED: 13 MAY 2005 <20050513/UP>
FILE COVERS 1976 TO DATE.

FILE CONFSCI
FILE COVERS 1973 TO 18 Mar 2005 (20050318/ED)

=>